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MEDICAL CARE OF WOUNDS CONTAMINATED WITH RADIOACTIVE MATERIALS

Asher J. Finkel, M.D.
and
Earl A. Hathaway, M.D., Lemont, Ill.

• *The presence of radioactive materials on the skin and in wounds introduces problems of therapy that heretofore have not complicated conventional surgical treatment. Attention to initial decontamination, adequate monitoring with special detection instruments, and possible excision of otherwise viable tissue may be necessary.*

Systemic injury, from the absorption of excessive amounts of radioactive substance, takes the form either of the acute radiation syndrome or of the delayed, varied toxic effects of slowly excreted, long-lived isotopes. Methods of hastening the excretion of some of these substances include the use of compounds such as zirconium citrate and edathamil calcium-disodium.

Elaborate decontamination facilities are necessary where radioactive materials are used, and the care of patients with contaminated wounds is made safer and more effective by suitable planning.

It is apparent that, in any organization concerned with nuclear energy, the possibility exists that ordinary traumatic injury will eventually coexist with contamination by radioactive materials. It would appear that this event would more probably occur in a research laboratory, where vast quantities of a variety of radioisotopes are used experimentally. Yet any organization utilizing a nuclear power source, a high-energy particle accelerator, or even just one isotope in a technical process or clinical procedure might subject its personnel to this risk. Indeed, during the past 12 years, several laboratories and institutions on the North American continent have on occasion been compelled to deal with this type of situation; their experience in such instances has been a major contribution to the ideas that are formulated here.

Radioactive materials may be accidentally introduced into the body by inhalation, ingestion, injection, percutaneous absorption, or contamination of wounds. The latter situation may result from penetrating wounds produced by contaminated objects or by surface contamination of an open wound. Radioactive substances may be readily absorbed from such wounds, and the amount or extent of such absorption depends on the physical and chemical characteristics of the radioisotope (e. g., ionic state, valence, physical state, solubility, pH), the nature of the wound (e. g., location, depth, area, vascularity of the tissue exposed, extent of tissue destruction), and the possible penetration of foreign material beyond the area of the wound. Additional factors include possible multiplicity of wounds, the time that has elapsed before treatment of the wound, and the effectiveness of preliminary decontamination of the wound. Whether a wound that has been contaminated with radioactive materials constitutes a danger to the individual depends on the purely "surgical" characteristics of the wound as well as on the complicating radiotoxic features that might exist.

Radiotoxicity of Internally Deposited Isotopes

The adverse effects of absorption and internal deposition of many radioelements depend upon a number of factors: the amount entering the body, the pattern of tissue distribution and retention, the radiation characteristics (nature and energy of the emanation, decay pattern, daughter isotopes), and the susceptibility of the tissues in which localization occurs (critical organ). The vast literature that has appeared in the past 10 years dealing with the metabolism of fission products, cyclotron-produced and reactor-produced isotopes, and many of the newer heavy elements can be referred to only cursorily here.[1]

Clearly, if excessive amounts of radioactive materials gain entrance into the body, there may be a real danger of the appearance of what is now called the acute radiation syndrome. This syndrome is characterized by an initial period of radiation illness, with prostration, vomit-

From the Health Division, Argonne National Laboratory.
This paper is based in part on a contribution to the Proceedings of the International Conference on the Peaceful Uses of Atomic Energy, Geneva, Switzerland, August, 1955.
Figure 6 is reprinted with permission from Renton.[12]

ing, diarrhea, and reduced food and water intake. The early phase of shock may be followed by a definitive period of acute radiation effects that are manifested chiefly by the more radiosensitive tissues of the body: the blood-forming organs, the gastrointestinal tract, and the gonads. White blood cell count depression, increased sedimentation rate, decreased gastric acidity, reduced glucose absorption by the intestines, and delayed emptying time of the intestines are some of the features of this period. Later features of the acute radiation syndrome are vasomotor collapse, emaciation, loss of hair, anemia, thrombocytopenia, increased bleeding tendency, and, terminally, widespread hemorrhages and generalized infection.

Delayed toxic effects may appear in survivors of the acute radiation syndrome or, more importantly for the present discussion, the toxic effects may be the consequence of internal deposition of slowly excreted, long-lived isotopes that are present in amounts insufficient to produce acute effects. Such elements are the "bone-seekers," such as radium, strontium, yttrium, cerium, uranium, and plutonium and other transuranic elements.[1c] Human cases of radium (and possibly also mesothorium) body burdens of the order of 0.7 to 23 mcg. have been found to be associated with spotty necrosis of bones, pathological fractures, and malignant bone tumors.[2] Malignant bone tumors have been found in rabbits given radium and mesothorium intravenously, in rats fed radium, and in rats surviving radioactive phosphorus (P^{32}) given intravenously.[3] Cancerous bone lesions have also been found in mice given small, single injections of such alpha-emitting elements as plutonium (Pu^{239}) (0.16 to 6.0 μc per kilogram), uranium (U^{232}) (1.0 to 10.0 μc per kilogram), and radium (Ra^{226}) (1.0 to 100 μc per kilogram).[4] Radio active strontium (Sr^{89}), a beta-emitting element that also becomes localized in bone, leads to malignant bone tumors in mice after single injections of 0.05 to 7.8 μc per gram.[3]

Neoplasms have also been experimentally produced in soft tissues. In rats, it has been found that polonium (Po^{210}) leads to tumors of the kidney and the adrenal gland and the ingestion of radioactive yttrium (Y^{91}) leads to adenocarcinomas of the colon. P^{32} has been found to be leukemogenic for mice, and in these animals liver adenomas have been produced by radiogold (Au^{198}) and functioning, transplantable pituitary tumors have been induced by radioactive iodine (I^{131}).[3] Considerations such as these, taken together with the wide variety of isotopes with differing chemical and radiation properties that may be encountered in industry and in the laboratory, make it essential that the immediate and long-term radiation effects be kept to a minimum.

Surgical Care and Considerations

If it can be safely assumed that the purely surgical problems created by such trauma can be dealt with successfully by employing the usual methods, three additional problems confront the physician: 1. What modifications of customary surgical technique must be used in coping with the complicating factor of radioactive contamination? 2. What specific and unique techniques are available for practical application to this special situation? 3. What physical facilities must be available to implement the solution of these problems?

The surgery of trauma depends upon the application of the following principles: asepsis, débridement of necrotic and severely damaged tissue, restoration of tissue continuity to preserve normal function and appearance, and consideration of the patient as a whole (shock, preexisting disease, metabolic needs, and prevention and treatment of infection). Of these considerations, it may be necessary to modify usual practices only as they relate to aseptic procedures and débridement. The usual technique of scrubbing the surgical field may remove pathogenic micro-organisms adequately, but it will not necessarily assure the maximum removal of radioactive contaminants on skin adjacent to the wound. Ordinarily, surgical preparation consists of shaving, scrubbing with gauze and antiseptic soap for a variable number of minutes, and applying an antiseptic solution to the surgical field. Decontamination of skin can be combined with this procedure by vigorous scrubbing with a nylon bristle brush for 10 to 30 minutes with sodium aryl alkyl sulfonate detergents rather than soaps and by much more frequent washing with water; shaving should be deferred until after removal of contaminating isotopes. If contamination is "fixed" to the skin, shaving should be omitted in order to prevent entry of radioactive materials through minute abrasions of the ordinarily intact skin barrier.

If definitive surgical care can be given immediately after an extremity wound is produced, absorption from the wound can be diminished by the application of an arterial tourniquet, especially if the radioactive contaminant is soluble in body fluids. However, the customary precautions must be exercised whenever such a device is used.

In some instances, depending on the chemistry of the contaminating substance, more effective removal is accomplished by conversion to a more soluble form, though in some instances this may facilitate percutaneous absorption. Some heavy metals, including uranium, form soluble complexes with the citrate ion, and some form soluble chelates with edathamil (ethylenediaminetetraacetate). Under some circumstances, the use of concentrated hydrochloric acid (about 8 *N*) is advantageous, especially in areas where the skin is thick and when the area of contamination is small. It is obviously important to conduct the decontamination of skin surfaces adjacent to wounds in such a way that the contaminating material is not introduced into the wound. This can be prevented by scrupulous attention to the mechanics of the scrubbing procedure, by possible preliminary suture of the wound, or by application of barriers. Cellophane surgical drapes can be so arranged that the wound is partially protected during the decontamination efforts. Repeated radiological monitoring of the involved areas throughout the procedures described should control the extent of the decontamination activities.

After the decontamination of adjacent skin, the wound itself must be thoroughly irrigated to accomplish removal of foreign substances. At present, isotonic sodium chloride solution, or its equivalent, is the only solution known to be safe for copious irrigation. It may be eventually shown that complexing or chelating solutions may be used as irrigants in special instances, although there are conceivable dangers of enhanced absorption if a soluble complex or chelate is formed.

Obvious necrotic and devitalized tissue must be surgically removed. As uncontaminated tissue is encountered during the débridement, contaminated surgical instruments should be discarded. Monitoring of the wound with radiation detection devices is required at this point as well as during the preliminary decontamination procedures. As an aid to determine whether radioactive material is present in the depths of a wound, Dr. Charles E. Miller, of the radiological physics division of Argonne National Laboratory, has devised sensitive scintillation-counter probes, some of which are no larger than a 14-gauge hypodermic needle (fig. 1). The tip of the probe can be introduced into the various recesses of the wound and is capable of detecting beta and gamma emanations over a wide range of energies. If necessary, the tip of the probe may be passed through intact skin and tissue to reach the vicinity of a foreign body previously localized radiographically. The probe, the photomultiplier assembly, and its cable may be subjected to sterilization to render them bacteriologically safe. Débridement of contaminated wounds may necessarily entail sacrifice of physiologically intact tissue if it appears that the future dangers resulting from retention of the contaminating material outweigh the immediate concern for satisfactory restoration of tissue continuity and function. Decisions to sacrifice restorable tissue must be made only after due consideration is given to the possibility and probability of delayed adverse effects from internally deposited isotopes. For example, the probable delayed toxic effect from 10 μc of Ra^{223} (11.2 days physical half-life) is considerably less than that from Ra^{226} (1,620 years half-life). These factors might be less important in the elderly because of shortened life expectancy with advancing age.

As for consideration of the best technique for removal of tiny amounts of contaminated materials from the skin (splinters or slivers), the sacrifice of a small amount of integument is frequently indicated. Block dissection is then performed and includes the tissues around the point of penetration of the foreign material. If this excision is accomplished expeditiously after injury, a more complete removal of radioactive contaminants is assured and less time is available for absorption and distribution of radioactive materials throughout the body.

When an injury has occurred, it becomes necessary to utilize all available techniques that will indicate accurately the extent to which absorption has occurred. All débrided material, surgical sponges, collected irrigating solutions, and instruments should be monitored for radioactivity. A venous blood sample should be withdrawn as soon as possible after the injury under conditions that will assure that no surface contamination is inadvertently introduced into the body by the venipuncture needle. This requires radiological survey of the venipuncture site and preparatory decontamination if necessary. The blood sample should be assayed promptly for the presence of radioactivity. Urine and fecal specimens should be collected daily as long as necessary and also subjected to assay.[5] If the absorbed material emits a suitable gamma ray, scintillation-counting methods may be used for external survey of the body to determine the probable body content and localization.[6]

In view of the very real dangers involved when radioelements enter the body, the concept of body burden (retained dose) has been devised. Bioassay techniques have been developed in an effort to appraise this amount, and maximum permissible levels have been set for radioisotope concentrations in urine and feces.[7] The published values refer largely to ingestion and inhalation as modes of entry into the body but are useful nevertheless in approaching the problems of wound contamination.

Medical Techniques for Increasing Excretion of Radioelements

Several nonsurgical techniques have been developed for hastening the elimination of radioactive isotopes from the body, especially when these are known to be or are suspected of being present in the body in hazardous quantities. The use of intravenously administered zirconium citrate to reduce tissue deposition of metallic radioelements was proposed by Schubert,[8] of Argonne National Laboratory, in 1949. The circulating radioelement is thought to be adsorbed by the zirconium colloid that forms in the blood at pH 7.4, and the combined zirconium-radioelement aggregate is carried out of the body via the urine. In experimental animals, the prompt administration of zirconium citrate or malate after single

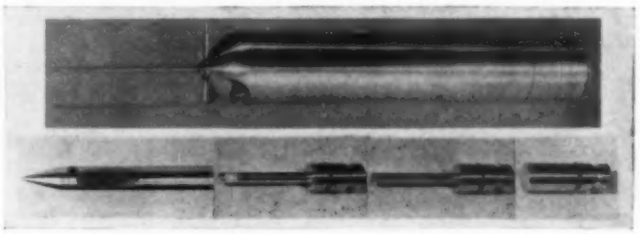

Fig. 1.—"Surgical scintillation-probe." The large handle portion contains the photomultiplier tube and preamplifier unit. The enlarged views show various exchangeable probes, with "windows" ground from 0.001 to 0.006 in. adjacent to the sodium iodide crystals.

injections of the radioelement has been found to reduce the subsequent bone content of Pu^{239} [9] and of Y^{91}.[8] On the other hand, there appears to be some as yet unpublished evidence for the occurrence of toxic side-effects with the administration of zirconium malate to humans. A further drawback to the use of zirconium therapy is that there appear to be difficulties with the stability of autoclaved preparations of zirconium citrate designed for use intravenously.

An entirely different approach to the treatment of heavy metal poisoning has been the use of the nontoxic compound edathamil calcium-disodium. This substance forms a soluble chelate with many heavy metals and rare earths; these include yttrium, lanthanum, iron, cobalt, zinc, cadmium, lead, nickel, copper, and, most important for nuclear reactor technology, plutonium and thorium.[10] Such soluble chelates are excreted unchanged by the kidneys, and the body burden is materially reduced, especially if the edathamil calcium-disodium is given promptly. Because of its high affinity for plasma calcium, the tetrasodium salt of edathamil cannot be used, since hypocalcemic tetany results from its administration. Reference must be made to the formation constants of the metal edathamil chelates in order to appraise the usefulness of this chelating agent in any specific situation. Thus, the formation constants for magnesium, strontium, barium, and presumably also radium salts of edathamil are somewhat below that of edathamil calcium-disodium.

Hence, the calcium in the latter compound will not be exchanged for these other alkaline earths in the blood, and the chelate is ineffective in removing them from the body. On the other hand, the formation constants for lanthanum edathamil and lead edathamil are roughly 10^5 and 10^8 times as large, respectively, as that for calcium edathamil, and accordingly calcium would be exchanged for these metal ions.

When given promptly, edathamil calcium-disodium was found by Foreman and others[10a] to increase substantially the elimination of plutonium from experimental animals, and this enhanced excretion led to reduced bone retention of plutonium, although the soft-tissue burden was not materially lowered. On the other hand, no effect was noted when treatment was delayed for 30 days. They found that treatment with edathamil calcium-disodium was effective in increasing the urinary excretion of plutonium in a laboratory technician who had sustained a hand laceration that was contaminated with plutonium. They also noted a substantial increase of urinary plutonium excretion when edathamil calcium-disodium treatment was instituted in a case where exposure to plutonium-containing vapors had occurred seven years earlier. Recent experimental work with rats suggests that prompt combined treatment with zirconium citrate and edathamil calcium-disodium is the most efficacious method of reducing the retained bone and soft-tissue burden of plutonium.[9b] An experience at Argonne National Laboratory indicated that administration of edathamil calcium-disodium intravenously increased the rate of urinary excretion of radioactive thorium (Th^{227}). This radioisotope entered the body of a technician through a puncture wound of the hand four days earlier.

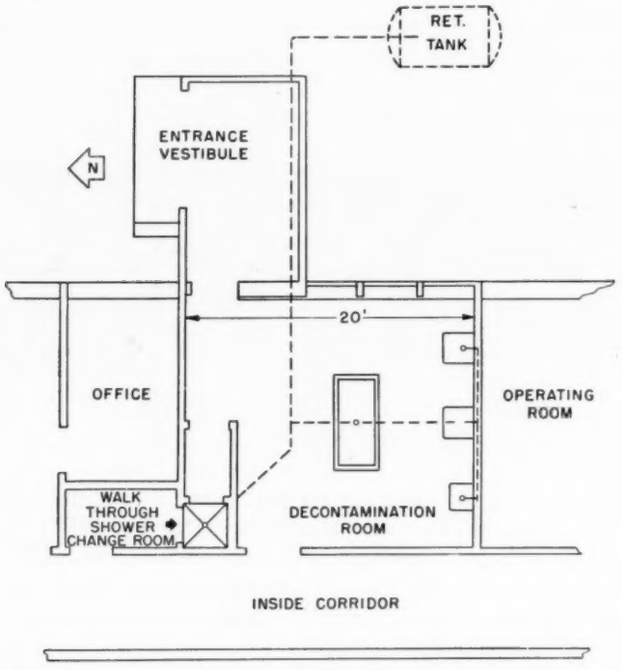

Fig. 2.—Floor plan of the decontamination-treatment room at Argonne National Laboratory. Dotted lines indicate the drainage flow to the retention tank buried outside the building.

The technique of isotope dilution may be utilized effectively in the special situation where tritium enters the body in the form of HTO. When this occurs, the tritium exchanges quickly with the hydrogen in body water[11] and body fluid levels of tritium may be estimated from assay of single urine specimens.[1b] The biological half-time of approximately 10 days can be reduced to two and one-half days by judicious water-loading of the patient, with consequent diuresis.[11] The same principle may be applied to the elution of radioactive sodium (Na^{24}) and potassium (K^{42}) from the body.

Special Treatment Facilities

Experience has shown that the administration of adequate medical and surgical care to the patient with coexisting radioactive contamination and trauma requires both specially designed physical facilities and special coordination of medical and ancillary personnel. This was first fully realized at the Canadian Chalk River Project of the Atomic Energy of Canada, Ltd., and the medical group there was the first to design and build such facilities.[12] The nature of the problem may be better appreciated if the following considerations are emphasized: 1. The patient may present the following degrees of contamination: (*a*) localized or general skin and clothing contamination with no trauma, (*b*) localized contamination of single or multiple wounds, (*c*) general skin and wound contamination. 2. Medical treatment facilities must not be rendered inoperative from generalized radioactive contamination of premises, equipment, and personnel after care of a single patient. 3. Medical and ancillary personnel must work safely and effectively without skin or internal contamination to themselves, or transmission of contamination from one patient to another, or risk of excessive exposure to external radiation.

The special arrangements in the main medical dispensary at Argonne National Laboratory are shown in figure 2, which illustrates the floor plan and entrance of a special facility known as the decontamination-treatment room. Figure 3 illustrates some of the features of this room. It is considered absolutely necessary that the known contaminated patient and assisting personnel, such as litter bearers, enter the dispensary by a separate entry provided for this purpose, so that spread of contamination to other parts of the building is precluded. The patient may be received by medical personnel directly from the vestibule, which is used for radiological monitoring purposes, removal of clothing, and transfer of the patient to a wheeled litter if necessary. The size of the decontamination-treatment room is sufficiently great to allow the admission of five mixed ambulatory or nonambulatory patients. Medical and radiological safety personnel within this room have the facilities and instruments available to estimate both the degree of physical injury and the nature and degree of radioactive contamination. In the center of the room is a fixed pedestal-type stainless steel autopsy table, which has been adapted for the decontamination and treatment of a nonambulatory patient. In addition to serving as an emergency major operating table, this fixture offers the additional advantage of allowing copious irrigation and cleansing of skin and wounds without spread of radioactive contamination to other parts of the room. Other stainless steel fixtures in the room for use by ambulatory patients include a special double-bowl sink at waist-level for treatment of hands and arms, and a special double-bowl sink

at knee-level for treatment of feet and legs. These have been adapted from commercially available physiotherapy units.

It is considered inadvisable to keep medical supplies stored within this room, inasmuch as they may become contaminated by handling. Accordingly, all medical and surgical supplies are kept in a storeroom adjacent to the decontamination-treatment room and are passed, as they are needed, into the treatment room through a split door. Individual packaging of instruments assures that a minimum of medical and surgical supplies are exposed to contamination in the course of any one surgical procedure; consequently, the conventional major or minor surgical "pack" is not used. Instruments are placed in a transparent plastic envelope and sterilized in the autoclave, and the envelope is then heat-sealed under sterile conditions. The envelope is a thermoplastic fluorocarbon film made of a commercially available polymer of trifluorochloroethylene and has the desirable properties of toughness, nonporosity, temperature-resistance, and inertness to strong chemicals (decontaminability). These properties make it possible to identify the contents readily, to maintain bacteriological sterility indefinitely, and to protect the contents against inadvertent contamination.

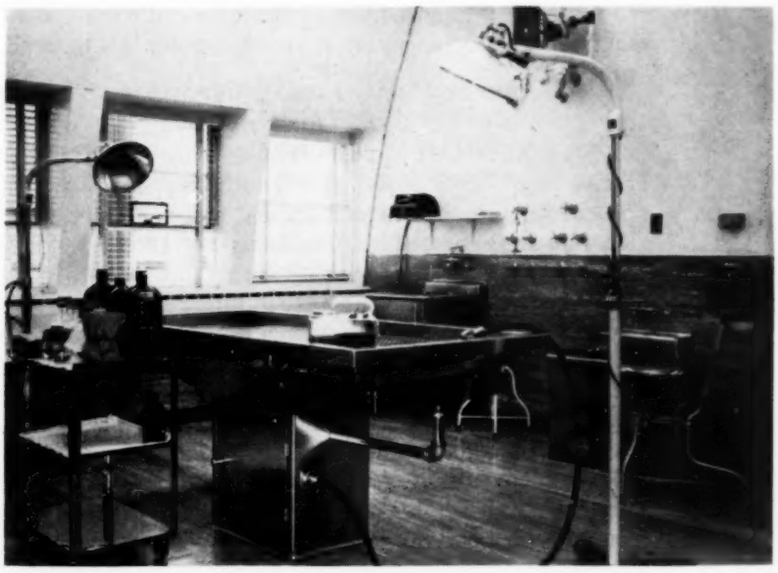

Fig. 3.—View from within decontamination-treatment room, showing treatment table and other decontamination equipment and fixtures.

All liquid wastes from the fixtures in this room drain into a 550-gallon (2,080 liter) retention tank buried in the ground outside the building. Before such wastes can be emptied into the public water-disposal system, they must be monitored to assure that permissible limits of activity are not exceeded. When the radioactivity of this waste exceeds set limits,[1c] the liquid is pumped out and disposed of by standard methods of liquid waste treatment. Similarly, the ventilation arrangements in this room are such that air flow cannot convey aerosols or gases into other areas of the building, even with the upper half of the split door open. Ducts in the ceiling exhaust air to the outside at the rate of approximately 20 room-air changes per hour. The walls, up to a level of 4.5 ft. (1.37 m.), and the floor are covered with ⅛ in. (3.2 mm.) thick sheet-vinyl floor-covering material that is impervious to penetration by strong chemicals and is easily decontaminable or, if necessary, readily replaceable. The upper walls and ceiling are painted with a vinyl plastic paint. After definitive treatment has been rendered, it may be necessary to transfer the patient to other parts of the dispensary for further medical care or to a hospital, or it may be possible to discharge him. The nonambulatory patient may be removed by a wheeled litter, which may be brought in, uncontaminated, from the main corridor of the dispensary after the floor area to be traversed is first covered with roll paper.

Medical and other personnel, if they have sustained some degree of skin and clothing contamination as a result of their treatment efforts, may discard their clothing by placing it in suitable dry-active-waste containers and may proceed to bathe in the shower; they may then leave the room through the special exit provided (fig. 2). The arrangement described and illustrated accomplishes the dual purpose of confining contamination problems to a limited portion of the medical facility and at the same time allowing considerable versatility in the approach to caring for the problem of coexisting trauma and radioactive contamination. The facilities are such that even major operative procedures with general anesthesia can be undertaken with full regard for the safety and welfare of the patient. The facilities are also such that, even under the worst imaginable conditions of radioactive contamination, medical personnel properly equipped with protective clothing and respirators could safely administer necessary care.

A more elaborate decontamination-treatment facility (fig. 4) was designed in 1952 by the Argonne National Laboratory medical staff, then under the direction of Dr. Robert J. Hasterlik. Attention should be directed to the proposed arrangements, which provide for decontamination and treatment by stages and for the traffic flow that makes this possible. Other laboratories on this continent

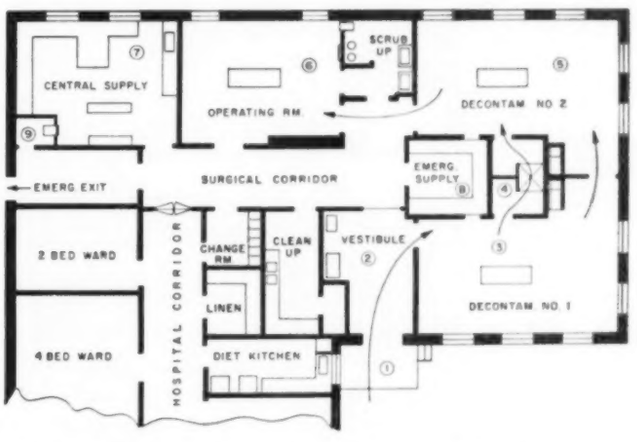

Fig. 4.—Floor plan of proposed Argonne National Laboratory decontamination suite: 1, receiving platform for contaminated patients; 2, vestibule for preliminary radiological monitoring; 3, decontamination room no. 1; 4, shower and clothing change area for medical personnel; 5, decontamination room no. 2. Beyond this point equipment and personnel are free from contamination; 6, operating suite; 7, central supply; 8, uncontaminated supplies pass outward from this room through pass windows; and 9, autoclave.

have developed their own solution to this problem by devising similar treatment arrangements. The facilities of the California Research and Development Company, Livermore, Calif., are shown in figure 5, which illustrates the floor plan of the decontamination facility and implies

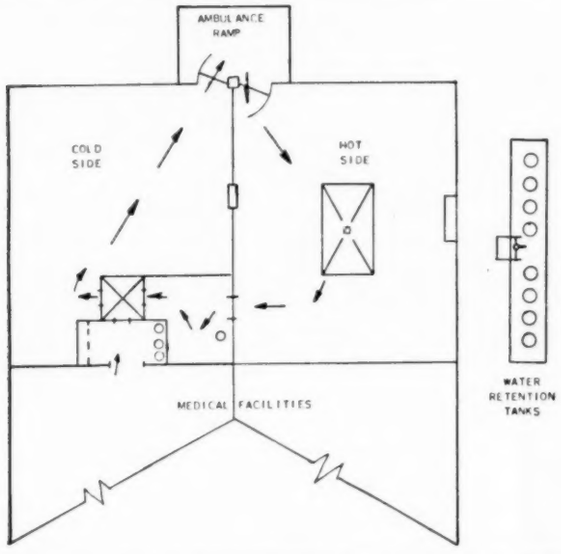

Fig. 5.—Floor plan of decontamination center at California Research and Development Laboratory, Livermore, Calif.

that decontamination procedures can be separated in both space and time from strictly medical procedures that would be done on the "cold side"—a view differing somewhat from our approach.[14] Figure 6 illustrates the floor plan of the decontamination unit at the Chalk River Project, Atomic Energy of Canada, Ltd.[12] The design of

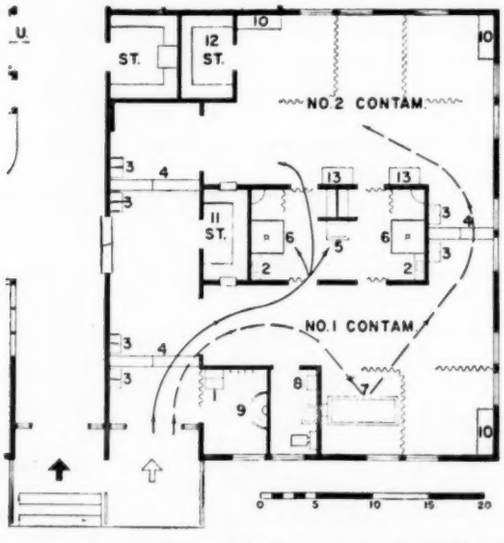

Fig. 6.—Floor plan of decontamination unit at the Chalk River Project, Atomic Energy of Canada, Ltd.: 1, hand and foot monitors; 2, portable monitors; 3, rubber stations; 4, hinged barriers; 5, scrub-up sink with shampoo attachment; 6, shower unit; 7, shallow bath; 8, lavatory with bedpan sterilizer; 9, foot-operated sink; 10, counter and cupboard; 11, emergency supplies (instruments, drugs); 12, reserve medical supplies; and 13, clothing stores.

this unit represents a most thorough and thoughtful effort on the part of the Chalk River Project medical staff to meet some of the problems discussed here.

In addition to physical facilities, it would be imprudent to leave unrecognized the importance of a fully trained and organized staff of personnel. It is apparent that the successful function of a decontamination-treatment facility depends upon the skilled and deliberate combined efforts of physicians and nurses cognizant of the problems of radioactive contamination, with assistance from qualified radiobiologists, chemists, and health physicists. All of these individuals must be familiar with the unusual medical techniques and procedures employed and must be aware of their purpose; only by such cooperative effort can an injured person exposed to radioactive contamination receive optimal treatment for his specific problems.

Summary

The medical care of wounds contaminated with radioactive materials is based on attention to special surgical procedures, the use of nonsurgical means of modifying internal deposition of radioelements, and the availability of special decontamination facilities designed to cope with the unique problems of such injuries. Special surgical procedures involve particular emphasis on adequate techniques designed to reduce and to limit extension of contamination, and they involve possible sacrifice of otherwise viable tissue because of fixed contamination. Judicious use of zirconium citrate and edathamil calcium-disodium intravenously may minimize the retention of selected, potentially toxic radioelements in the body. Finally, the physical design of several decontamination-treatment rooms is related to the problems of these injuries occurring in atomic energy establishments.

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ANDROGEN-INDUCED EXACERBATION OF BREAST CANCER MEASURED BY CALCIUM EXCRETION

CONVERSION OF ANDROGEN TO ESTROGEN AS A POSSIBLE UNDERLYING MECHANISM

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• *Responses to the administration of androgens and estrogens were studied in four women in whom there was cancer of the breast with bony metastases. On the basis of the idea that active growth of tumor in bone results in liberation of calcium secondary to increased osteolysis, the responses of the tumor to these hormones were measured by changes in the level of serum calcium and in calcium excretion. Hypercalcemia and hypercalcuria developed after administration of both hormones, and urinary calcium measurements proved to be an excellent guide to impending hypercalcemia. It is concluded that either estrogen or androgen may stimulate the growth of mammary cancer and that a possible mechanism underlying this observation is the conversion of androgen to estrogen in the human.*

Human breast cancer has been characterized on the basis of its responsiveness to estrogen administration and to endogenous estrogen withdrawal, that is, castration and adrenalectomy. In a group of patients reported on by Pearson and others,[1] the response rate following castration in premenopausal women and adrenalectomy in premenopausal and postmenopausal women was about 45% (table 1). In these patients mammary carcinoma was classified as dependent upon estrogen only if there was objective regression of disease. In patients with estrogen-dependent tumors, testosterone might be expected to suppress the tumor growth if it exerts its beneficial effects by opposing the action of endogenously produced estrogen. However, it is known to induce objective suppression of tumor growth in only about 20 to 25% of all women with breast cancer [2] (table 1). Hence, about half of those who might be expected to respond to testosterone on the basis of estrogen antagonism fail to do so. In those who fail to respond to testosterone, some may experience actual acceleration of their disease.[3] The reasons underlying these observations have been obscure.

It is the purpose of this study to report the cases of four patients with breast cancer and osseous metastases whose disease was exacerbated by androgen therapy and to describe a possible mechanism underlying this stimulation of the growth of breast cancer. Acceleration in the growth of skeletal metastases was measured by following the levels of serum and urinary calcium. The development of hypercalcuria or hypercalcemia during hormone therapy was regarded as secondary to progression of tumor growth with "a flooding of the circulation by the products of osteolysis." [3] Determination of serial changes in serum and urinary calcium has been described [4] as a means of demonstrating, objectively, changes in tumor growth.

Clinical Material and Methods

Four women with breast cancer and bony metastases were studied. Their ages, the duration of disease, and previous therapy are summarized in table 2. The patients in cases 1 and 2 were hospitalized on the metabolic ward during the study and were on limited ward activity. Measurements of urinary calcium were made daily in these two patients. Urinary calcium was measured by the method of Fiske and Logan.[5] Serum calcium was analyzed by the method of Clarke and Collip, serum phosphorus by the method of Fiske and Subbarow, and serum alkaline phosphatase by the method of Bodansky. These serum determinations were carried out two or three times weekly, as were hematocrit readings and platelet counts. Data on vaginal smears were obtained by Dr. John Finkbeiner. The measurements were made before, during, and after therapeutic trials with androgen and estrogen therapy. A urinary calcium excretion of 150 mg. per day or more was regarded as abnormal, inasmuch as the dietary intake of calcium was restricted to 200 mg. per day or less. A range in serum calcium values of 9.2 to 10.8 mg. per 100 cc. was regarded as normal.

TABLE 1.—*Response to Estrogen Administration and to Endogenous Estrogen Withdrawal**

	Premenopausal		Postmenopausal		All-Inclusive	
	No. of Cases	Objective Responses, %	No. of Cases	Objective Responses, %	No. of Cases	Objective Responses, %
Castration	75	44	21	10	96	36
Adrenalectomy	..	..	..	..	384	45
Androgen	54	13	113	20	167	18

* Data from Pearson and co-workers.[1]
† These patients had all previously been oophorectomized.

All of the patients had undergone previous radical mastectomies, and two of the four patients had had prior castration (table 2). None had undergone adrenalectomy. Other forms of therapy and associated responses are summarized in the table. All women were premenopausal at the time of onset of their disease, which varied in duration from 17 to 68 months. In three patients

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Drs. H. T. Randall, J. Urban, and G. Escher, of Memorial Center for Cancer and Allied Diseases, referred the patients studied.

(cases 1, 2, and 3) the clinically detectable disease was confined to the skeleton at the time these observations were made. The patient in case 4 had, in addition, evidence of pulmonary metastases.

Report of Cases

CASE 1.—A 48-year-old married woman had osseous metastases that were observed six months after mastectomy. Treatment at that time included castration by x-ray, followed by ad-

TABLE 2.—*Data on Women with Breast Cancer and Bony Metastases*

Case No.	Age, Yr.	Duration of Disease, Mo.	Previous Therapy *					Response to Previous Therapy
			Mastectomy	Castration	Androgen	Cortisone	X-Ray Therapy	
1	48	17	Left radical 3 mo. after onset	X-ray, 6 mo. before study	Methyltestosterone for 3½ mo. then testosterone propionate for 7 wk. (up to study)	Orally 50 mg. daily for 2 mo. (up to study)	To lesions in dorsal spine	Partial response to castration—relapse in 2-3 mo.; androgen caused hypercalcemia; no response to cortisone; relief of pain with x-ray
2	35	27	Right radical 6 mo. after onset	No	No	Orally 300 mg. daily for 5-6 wk. (up to study)	No	Marked subjective improvement on cortisone therapy, hemolytic aspects of myelophthisic anemia disappeared on cortisone therapy
3	50	60	Left radical 3 days after onset	Surgical, 6 wk. before study	No	No	To lesions in lumbar and sacral spine	Partial response to castration; urine calcium level decreased, but bone pain and evidence of spread on skeletal survey led to androgen therapy 6 wk. later; relief of pain with x-ray therapy
4	46	68	Right radical 5-6 wk. after onset	No	Testosterone propionate for 4 mo.	No	No	Initial improvement symptomatically, but disease relapsed under therapy; androgen therapy stopped 3 mo. before estrogen therapy started

* No adrenalectomies had been performed, and none had received previous estrogen therapy.

TABLE 3.—*Response to Androgen*

Case No.	Amount and Duration of Testosterone Propionate Therapy	Maximum Changes in Calcium			
		Urine Calcium, Mg./24 Hr.	Time of Observed Change	Blood Calcium, Mg./100 Cc.	Time of Observed Change
1	1,100 mg. total (50 mg. I.M. daily for 22 days)	30	Control	9.2	Control
		570	18 days after androgen therapy was stopped	15.3	14 days after androgen therapy was stopped
		52	34 days after androgen therapy was stopped	10.7	24 days after androgen therapy was stopped
2	1,750 mg. total (50 mg. I.M. daily over 36-day period)	60	Control	10.1	Control
		628	On last day of therapy	12.8	2 days after androgen therapy was stopped
		27	11 days after androgen therapy was stopped	10.6	6 days after androgen therapy was stopped
3	1,100 mg. total (100 mg. I.M. 3 times a week over 23-day period)	78	Control	...	.....
		233	On day 16 of androgen therapy	10.6	On day 19 of androgen therapy
		131	3 days after androgen therapy was stopped	...	.....
		96	17 days after androgen therapy was stopped	...	.....
4	400 mg. total (100 mg. I.M. 3 times a week over 9-day period)	..	.....	12.3	Control
		706	10 days after androgen therapy was stopped	22.5	On day 7 of androgen therapy
		73	16 days after androgen therapy was stopped	10.7	14 days after androgen therapy was stopped

TABLE 4.—*Response to Estrogen*

Case No.	Amount and Duration of Estrogen Therapy	Maximum Changes in Calcium			
		Urine Calcium, Mg./24 Hr.	Time of Observed Change	Blood Calcium, Mg./100 Cc.	Time of Observed Change
1	Ethinyl estradiol (Estinyl), 1.5 mg. total (in divided doses over 13-day period)	70	Control	9.2	Control
		454	14 days after estrogen therapy was stopped	13.2	9 days after estrogen therapy was stopped
		184	46 days after estrogen therapy was stopped	10.7	15 days after estrogen therapy was stopped
2	Free estradiol, 19 mg. total (1 mg./day I.M. over 19-day period)	55	Control	10.2	Control
		218	3 days after estrogen therapy was stopped	11.4	11 days after estrogen therapy was stopped
		42	13 days after estrogen therapy was stopped	8.8	39 days after estrogen therapy was stopped *
3	Ethinyl estradiol, 0.2 mg. total (0.05 mg. twice a day over 2 days)	173	Control	11.2	Control
		343	3 days after estrogen therapy was stopped	...	.....
		66	28 days after estrogen therapy was stopped	10.5	14 days after estrogen therapy was stopped
4	Estrogenic substances, conjugated (Premarin), 480 mg. total (10 mg. 3 times a day over 16-day period)	..	.....	10.3	Control
		..	.....	13.5	On day 15 of therapy
		..	.....	10.7	8 days after estrogen therapy was stopped

* No serum calcium determination was made in the interval between 11 and 39 days after estrogen therapy was stopped.

ministration of androgen and cortisone. The reported observations were begun at the conclusion of this latter therapy. The results are summarized in tables 3 and 4 and illustrated in figure 1. Initially the patient was recovering from hypercalcemia experienced during a prior course of therapy with testosterone propionate given in conjunction with cortisone. When her condition had stabilized after termination of this treatment, administration of 50 mg. of testosterone propionate given intramuscularly daily was resumed, and she received a total of 1,100 mg. over a period of 22 days. The urinary calcium level rose from control values of 30 mg. per 24 hours to 570 mg. per 24 hours and returned to control levels two weeks after this peak. The serum calcium level rose transiently from normal to 15.3 mg. per 100 cc. two weeks after testosterone therapy had been stopped. Following a period when both urine and serum calcium values remained at normal levels, the patient was given a total of 1.5 mg. of ethinyl estradiol orally over a 13-day period. Hypercalcemia (to 13.2 mg. per 100 cc.) and hypercalcuria (to 454 mg. per 24 hours) were again observed. An increase in the percentage of cornified cells in the vaginal smear to 60% was noted during the administration of estrogen, but no rise was seen with androgen therapy. Surgical castration and adrenalectomy were subsequently advised, but the patient refused. She died about five months later.

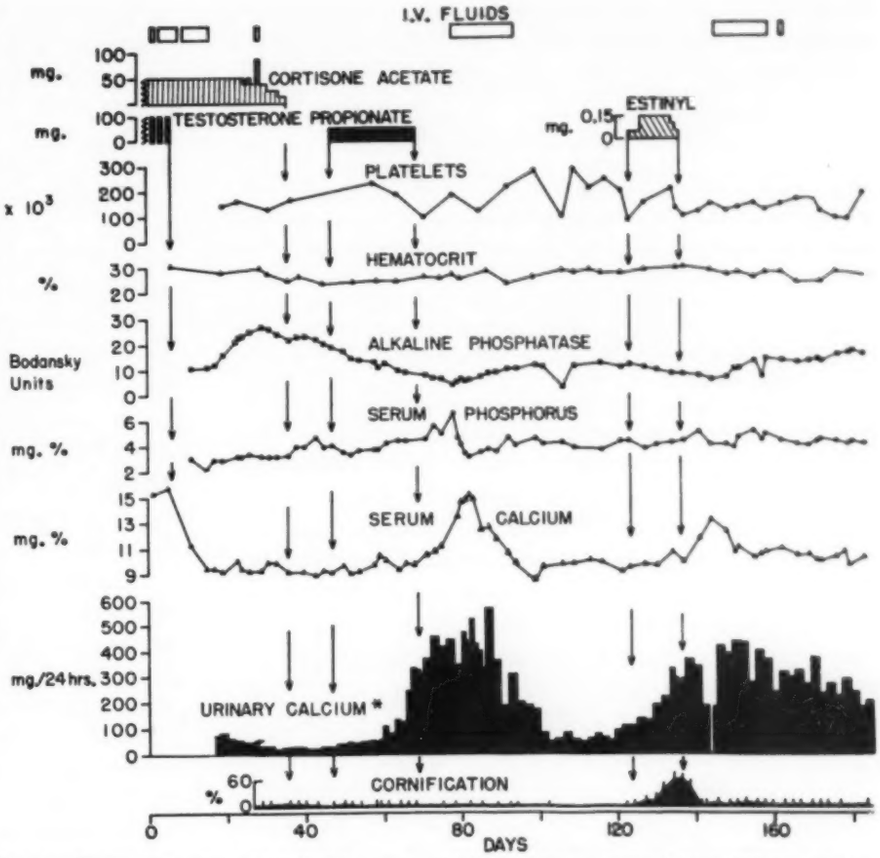

Fig. 1.—Results of treatment of patient in case 1. Calcium intake was approximately 200 mg. per day.

CASE 2.—A 35-year-old woman had bony metastases noted 22 months after a radical mastectomy. At that time, because of a severe myelophthisic anemia, the patient was started on cortisone therapy. There was definite subjective improvement, and the signs of hemolysis disappeared. Our observations were started at this point. The data are summarized in tables 3 and 4 and illustrated in figure 2. The patient received a total of 1,750 mg. of testosterone propionate intramuscularly over a 36-day period. The urinary calcium level rose from control levels (60 mg. per 24 hours) to a peak of 628 mg. per 24 hours on the last day of administration of testosterone. It returned promptly to control levels after termination of treatment. The serum calcium level rose transiently to 12.8 mg. per 100 cc. This exacerbation was entirely a chemical one, as the patient experienced no symptoms of advancing disease or of hypercalcemia. With the reversal of these calcium changes, a "flare" [6] in the level of alkaline phosphatase was observed. Subsequently the patient was treated with estradiol given intramuscularly. Therapy was begun five days after completion of x-ray castration and was continued at a dose of 1 mg. per day for 19 days. Again hypercalcuria and hypercalcemia were observed. The percentage of cornified cells increased to 26% during the course of estrogen therapy, but no rise was observed with testosterone therapy. The patient subsequently experienced a remission lasting five months as a result of x-ray castration and was able to return to her full activities as a housewife and mother.

CASES 3 and 4.—The data obtained on the patients in cases 3 and 4 are less complete, inasmuch as urinary calcium values were not determined each day, and in case 4 no determinations of urinary calcium values were made during estrogen therapy. However, the data as summarized in tables 3 and 4 do indi-

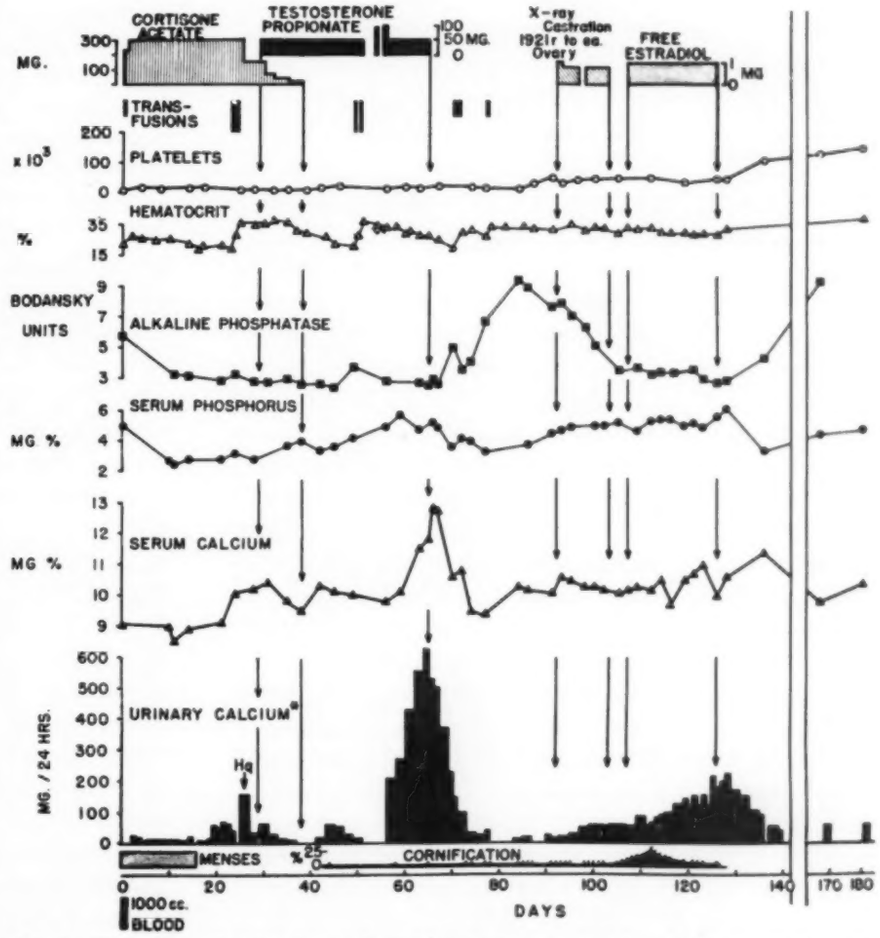

Fig. 2.—Observations of patient in case 2. Calcium intake was approximately 200 mg. per day. Hg refers to mercurial diuretic given on day indicated.

cate (1) that hypercalcuria developed in the patient in case 3 with both androgen and estrogen therapy and that this reverted to normal levels after the hormones were discontinued and (2) that transient hypercalcemia developed in the patient in case 4 during therapy with androgen and estrogen. The patient in case 4 had an elevated serum calcium level before testosterone was administered, and the data might therefore be interpreted as indicating a spontaneous exacerbation rather than a testosterone-induced one. However, the rapid increase in the serum calcium level following the administration of testosterone plus the prompt return to normocalcemic levels following cessation of therapy point to testosterone acceleration as the most important cause of the changes observed. Unfortunately, a control urine calcium value was not obtained in this patient. However, a urinary calcium value was observed to be 706 mg. per 24 hours 10 days after testosterone therapy had been stopped, and 16 days afterward it had returned to normal levels. These data afford additional support that this was a testosterone-induced exacerbation.

Comment

These studies raise two important problems. We wish to consider first the complication of hypercalcemia per se and, second, the reasons underlying the increased tumor growth that the hypercalcemia reflects. The use of androgens in the treatment of osseous mammary cancer [7] has led to the recognition of hypercalcemia as a complication of such therapy, and reports indicate that it occurs in about 10% of patients.[8] Despite this increased recognition,[9] fatal hypercalcemia may develop because of difficulties in its early detection. Lewison,[10] in considering breast cancer and its hormonal treatment, has commented on the difficulties involved in anticipating the development of hypercalcemia during the course of treatment with hormones. Two of the cases (cases 1 and 2, fig. 1 and 2) demonstrate a possible answer to this dilemma. In both patients the urinary calcium data proved to be of great usefulness in the early recognition of this problem. Table 5 shows the urinary calcium values that led to the discontinuance of therapy in these two patients and the simultaneous serum calcium values. In only one instance was the serum calcium slightly above normal. Neither patient had any warning symptoms of impending hypercalcemia, and the steroid therapy was discontinued solely on the basis of the rising excretion of calcium in the urine. In patients whose renal function is known to be adequate, and who have normal pretreatment serum calcium levels, the frequent determination of urinary calcium levels during hormonal therapy affords a better guide to impending hypercalcemia than any other chemical test. However, in patients who have definitely abnormal renal function, the serum calcium level must be determined in conjunction with the urinary calcium, since in this setting the latter may not provide a guide to impending hypercalcemia. The patient in case 1 demonstrates the point that the serum calcium level may continue to rise for several days despite cessation of therapy. If the serum calcium level had been the only guide in deciding when to stop testosterone therapy in this patient, it is entirely possible that, with the subsequent rise, the serum calcium might have reached a fatal level. Some authors [8] feel that androgen treatment may be tried again after correction of induced hypercalcemia, since patients so treated have subsequently been improved without recurrence of hypercalcemia. The explanation of this is not known. We feel that the offending hormone should not be tried again unless the disease is progressing in spite of all treatment alternatives.

TABLE 5.—*Urinary and Serum Calcium Values*

Case No.	Therapy	Urinary Calcium, Mg./24 Hr.*	Serum Calcium, Mg./100 Cc.
1.....	Estrogen	294	10.7
	Androgen	338	9.8
2.....	Estrogen	152†	11.0
	Androgen	430	10.2

* Amounts listed are those that guided therapeutic decisions; they do not coincide with the values on the last day of treatment, since there was a delay of 24 to 36 hr. between collecting a specimen and obtaining the calcium value.

† This value was regarded as abnormal, since it represented a threefold increase over control values.

The four patients presented all exhibited evidence of acceleration of tumor growth (as judged by calcium studies) when both estrogen and androgen were administered. As stated earlier, it might be supposed that androgen (testosterone) would have benefited these patients if its action is to oppose endogenous estrogen. Yet, as shown above, only about half of those women known to have estrogen-dependent breast cancer experience objective responses to testosterone. The reasons underlying the failure of androgen to cause tumor suppression in a higher percentage of cases and the mechanisms involved in androgen exacerbation have been speculated upon for some time. Steinach and his colleagues [11] have demonstrated that the administration of androsterone to rats was followed by an increased excretion of biologically active estrogen in the urine. Later studies showed rises in urinary estrogen when androgens were administered to normal as well as to castrated men. Nathanson and coworkers [12] have reported increased excretion of estrogens in two patients with breast carcinoma under treatment with androgen. Nathanson and Kelley [2] have written that this rise in urinary estrogens "suggests that, under some circumstances, at least, androgens are involved in increased estrogen production" and that "this might help to explain the favorable effects on soft-tissue breast lesions occasionally seen in postmenopausal women" (treated with androgens). Inasmuch as the urinary estrogens found by these investigators might have originated in the adrenal glands, one of us (C. D. W.) has studied urinary estrogens in two castrated, adrenalectomized women.[13] Tests of control urines revealed no measurable urinary estrogens. When testosterone propionate was administered to these women, estrone and estradiol were identified in the urine by countercurrent distribution and paper chromatography. Since both patients were castrated and adrenalectomized, one of us (C. D. W.) concluded that the administered testosterone was metabolized in part to estrone and estradiol.

Although we do not have data on urinary estrogen excretion in the patients here reported, it seems reasonable to speculate, in view of the above studies, that the ad-

ministered androgen was in part converted to active estrogenic substances and that this conversion accounted for the exacerbation of tumor growth. No estrogenic effects were observed in the vaginal smears of two patients (cases 1 and 2) taken during androgen therapy, while increased cornification was noted during treatment with estrogens. This finding does not preclude the possibility of conversion of androgen to estrogen, since the quantity of estrogen necessary for vaginal cornification may bear no relation to that necessary for stimulation of tumor growth. Conversion of androgen to estrogen might also provide an explanation for the failure of testosterone therapy to induce a higher percentage of remissions in women with estrogen-dependent breast cancer.

Such a proposed mechanism immediately raises certain questions. Presumably all women are capable of converting androgen to estrogen, and one of us (C. D. W.) [13] has shown that it is possible for a patient to improve on testosterone therapy despite conversion, in part, of this testosterone to estrogen. Why, then, do some women with estrogen-dependent cancer improve on testosterone therapy, while others are unimproved or made worse by it? A partial explanation may be in the quantities of androgen administered relative to those of estrogen formed. The effects of a given amount of estrogen will vary in different tissues according to different gradients of response.[14] Likewise the reversibility of such effects by androgens might be expected to vary from tissue to tissue. Possibly, then, the androgen administered to patients with breast cancer might be sufficient to reverse the effects of the estrogen metabolite in some women, whereas the ratios of these two hormones might be such in other patients that the effects of estrogen prevail and exacerbation results.

Another point that arises in this connection is the difference in the incidence rate of hypercalcemia induced by androgen and by estrogen. If hypercalcemia is indicative of accelerated tumor growth in bone (as we believe it is) and if androgen causes such acceleration by conversion to estrogen, it might be supposed that the incidence of hypercalcemia would be about the same for the two hormones when used in the treatment of patients with osseous disease. Yet in a series of 84 patients with bone metastases treated with estrogens, hypercalcemia was observed in only 2 patients, whereas it occurred in 7 of 97 patients with bone metastases treated with androgens.[8b] This difference, however, may not be valid, since those patients receiving estrogens were probably postmenopausal and those receiving androgens premenopausal. Further analysis would require a study of comparable groups.

Another possible explanation for androgen exacerbation of breast cancer, aside from the proposed conversion to estrogen, is that androgens may directly stimulate mammary cancer. It must be considered that a breast cancer cell, abnormal in so many respects in relation to normal breast tissue, may in some instances have lost its ability to distinguish between androgen and estrogen. In such cases the cell might thrive on any gonadal steroid.

Hence, although the evidence is suggestive that conversion of androgen to estrogen is responsible for androgen exacerbation of human mammary carcinoma, it is by no means conclusive, and there are reasonable objections and alternative explanations that demand further study.

Summary and Conclusions

Exacerbation of metastatic mammary cancer in bone has been observed in four patients during treatment with androgen. Tumor growth in each patient was stimulated also by the administration of estrogen. These four patients had hypercalcemia and/or hypercalcuria secondary to increased osteolysis due to accelerated tumor growth. Urinary calcium data are an important guide to the early recognition of impending hypercalcemia.

The demonstration of the estrogens estrone and estradiol in the urine of two castrated, adrenalectomized women with breast cancer while under treatment with androgen has been related to the problem of androgen exacerbation. The conversion of androgen to estrogen in women may be a possible mechanism underlying androgen exacerbation of human mammary cancer.

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TREATMENT OF POSTURAL HYPOTENSION WITH A COUNTER-PRESSURE GARMENT

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• *Two types of garments designed to apply counter-pressure over the body from the waist down were tried in 10 patients with severe postural hypotension. In two cases the condition followed bilateral sympathectomy for hypertension; in the others it was either idiopathic or associated with diabetes mellitus. One patient could not sit up without fainting, and six others had frequent or occasional episodes of syncope on standing.*

The air-filled suit was generally more effective than the elastic form of garment. The beneficial effects were explained by the increases observed in the blood pressure and cardiac output, which were measured on a tilting table.

Four patients were able to return to part-time employment. They found the suit both practical and comfortable and could do work that involved longer periods of standing than they had been able to endure before.

Postural hypotension may be a chronic, distressing, and disabling illness that is difficult to treat. The marked postural fall in blood pressure observed in this situation results primarily from the inability of the peripheral arteries to constrict and maintain arterial resistance when the patient stands.[1] A decrease in cardiac output [2] and impairment of venomotor activity, with decreased venous return to the heart [3] during standing, may also contribute to orthostatic hypotension.

In general, therapy of this syndrome has consisted in the use of vasoconstrictor drugs, attempts at increasing the blood volume, and the use of elastic stockings and abdominal binders. Vasoconstrictor drugs, while of value, are not usually successful in relieving symptoms in severe cases.[4] Increasing the blood volume by infusions temporarily prevents the fall in blood pressure during standing.[5] The administration of salt and desoxycorticosterone has been reported to aid in maintaining blood pressure presumably by increasing the blood volume.[6] Previous studies have demonstrated that pressure applied to the lower half of the body by immersion in water will prevent the postural fall in arterial pressure with its associated symptoms.[1b] The development of new materials and advances in garment design have now allowed the fabrication of an elastic suit that can apply effective pressure without being inordinately restrictive. It is the purpose of this report to describe results obtained with the use of such a suit in the treatment of postural hypotension, together with some observations on the mechanisms by which the suit helps to support the arterial blood pressure in the erect position.

Methods

In the 10 patients who were subjects for the study, postural hypotension was idiopathic in 4, associated with diabetes mellitus in 4, and followed bilateral sympathectomy for hypertension in 2. In all cases initial experiments were done with an air-filled garment to apply pressure during passive standing. This garment consisted of neoprene-impregnated nylon trousers that enclosed the feet and reflected inward over the abdomen at the waist to form a double wall.[7] The trousers were made air tight by rubber seals at the upper thigh. After control studies, air pressure of 25 to 30 mm. Hg was maintained in the trousers during observation in the recumbent and tilted positions.

Individually tailored pressure garments were fabricated for 6 of the 10 patients. The garments consisted of elastic knit cloth trousers and were tailored to apply up to 25 to 30 mm. Hg pressure over the lower half of the body, from the ankles to the waist. A lightweight vest was attached to the trousers to make a one-piece garment (fig. 1). Zippers were inserted in the front of the trunk and on the side of each leg to aid in donning the suit. The cotton-rayon elastic knit cloth was porous and lightweight. With frequent washing, it maintained its original elasticity for many months. The elastic pressure garment was worn frequently by these subjects during their waking hours for periods up to 24 months.

Initial observations were made with the patient on a tilting table in the supine position and at a foot-down angle 35 to 60 degrees from horizontal. Arterial pressure was recorded from the brachial artery through an indwelling needle by means of a strain gauge and direct-writer recording device. The point of zero reference was 5 cm. below the fourth costochondral junction in the supine position and at the fourth costochondral junction in the upright position. The same technique was used for measuring pulmonary arterial pressure through an intracardiac catheter. The cardiac output was estimated by the Fick principle after intracardiac catheterization.[8] Mixed venous blood was obtained from the atrium or the pulmonary artery; arterial blood, from the brachial artery through the indwelling needle. Blood oxygen contents were determined by a spectrophotometer method.[9] Arteriovenous oxygen differences determined at the beginning and at the end of the timed collection of expired air checked within 5%. Repeated measurements of the arteriovenous difference were considered necessary to establish that the subject had attained a suffi-

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The garments used in this study were designed and fabricated by the David Clark Company, Inc., Worcester, Mass.

ciently steady state to permit reliable estimate of the cardiac output by the Fick method. Oxygen consumption was measured by timed collection of expired air in Douglas bags, with subsequent gas analysis and volume measurement.

The cardiac output and intravascular pressures were measured with the patient supine and during a six-to-eight minute period of 35 degrees to 60 degrees foot-down tilt without and with support by a pressure garment. A period of three to four minutes immediately after the tilt was allowed to elapse before measurements were begun.

"Calculated resistance" was determined in four patients without and with counterpressure and was expressed as the ratio between mean arterial pressure in millimeters of mercury and cardiac index in liters per minute per square meter of body surface. A rise in this function is taken to indicate an over-all narrowing of the arteriolar bed, while a fall suggests dilatation. It is probable that this interpretation is not entirely correct,[10] but it is believed that changes in calculated resistances are primarily determined by changes in arteriolar caliber.

Results

In general, the air-filled suit provided greater and more consistent protection than did the elastic garment. This was to be expected, because the elastic garment was intentionally designed to sacrifice to some degree the amount of pressure and the uniformity of its application in favor of comfort. The extent to which the arterial pressure could be supported by the air suit is detailed in table 1. Data on the protection afforded by the elastic garment are presented in table 2. The arterial pressures represent typical responses for each patient while recumbent and when tilted without and with a counterpressure garment. Although the postural fall in pressure was not completely prevented by pressure garments, it was always less than during the tilt without counterpressure. All of the patients had relief of the symptoms associated with tilting when a pressure garment was used. It should be noted that the degree of postural hypotension and associated symptoms may vary in a particular patient, depending on the apprehension of the patient, his activity, the environmental temperature, and probably other factors as well. Similarly, the degree of protection afforded by the counterpressure garment varied and depended to some extent on these factors.

Individually tailored elastic pressure suits were fabricated for six of the group to use daily at home. In the other four patients associated illnesses made it impossible for them to use the suit and resume any normal activity. Four patients were able to return to part-time employment and to carry on daily activities entailing periods of standing that were impossible before use of the pressure suit was started. They found the suit both practical and comfortable.

Two patients (L. M. and A. M.) had been incapacitated by orthostatic hypotension following partial ablation of the sympathetic nervous system for hypertension. In these cases the suit not only provided some immediate protection but its use was also associated with gradual, but marked, diminishment in the severity of postural hypotension. L. M., a 52-year-old man, was bedridden, depressed, anoretic, markedly underweight, and totally

TABEL 1.—*Typical Arterial Pressure Changes During Tilt of All Patients Using the Air-Filled Suit*

Date	Patient	Sex	Age	Diagnosis	Symptoms with Standing	Arterial Pressure, Mm. Hg		
						Supine	Tilt Without Counter-pressure *	Tilt With Counter-pressure *
8/11/52	A. M.	F	40	Postural hypotension following sympathectomy for hypertension	Sweating; weakness; syncope after 3 to 5 minutes	178/110	80/60	168/118
11/22/52	W. W.	M	41	Postural hypotension, diabetes mellitus	Blurred vision; occasional episodes of syncope	130/90	60/50	90/78
12/16/52	M. B.	M	53	Postural hypotension, idiopathic	Sweating; weakness; frequent episodes of syncope	130/75	55/45	94/72
9/13/53	E. H.	M	42	Postural hypotension, diabetes mellitus	Weakness; lightheaded after 2 to 3 minutes	124/76	75/60	104/82
10/20/53	L. M.	M	52	Postural hypotension following sympathectomy for hypertension	Marked weakness; sweating; syncope after 2 to 3 minutes	114/78	48/42	110/80
10/26/53	S. W.	M	49	Postural hypotension; diabetes mellitus	Weakness	118/82	92/72	120/89
11/13/53	W. N.	M	65	Postural hypotension, idiopathic; renal disease; bladder neck obstruction; mild uremia	Sweating; weakness; episodes of syncope	114/76	68/55	80/60
3/ 3/54	C. W.	M	69	Postural hypotension, idiopathic	Sweating; headache; weakness; blurred vision	110/60	60/46	104/82
11/12/54	E. L.	F	46	Postural hypotension, idiopathic	Weakness; frequent episodes of syncope; convulsions	90/68	40/30	92/74
12/14/54	J. S.	M	31	Postural hypotension, diabetes mellitus	Weakness; occasional episodes of syncope	100/70	50/30	104/72

* The patient was tilted at an angle of 30 to 60 degrees for from 2 to 4 minutes. The counterpressure was supplied by the air-filled suit.

TABLE 2.—*Typical Arterial Pressure Changes During Tilt of Patients Using the Elastic Pressure Suit*

Date	Patient	Arterial Pressure, Mm. Hg		
		Supine	Without Counter-pressure *	With Elastic Pressure Suit *
2/ 6/53	A. M.	190/110	100/70	130/90
12/ 9/53	L. M.	140/80	58/48	80/58
3/24/54	C. W.	112/74	74/58	122/88
3/25/54	E. H.	135/77	96/60	102/70
7/ 8/54	M. B.	120/90	52/44	76/58
12/16/54	J. S.	122/88	92/62	112/82

* The patients were tilted at an angle of from 30 to 60 degrees for from 2 to 4 minutes.

incapacitated for six months. He could not stand or sit without syncope or presyncopal symptoms. With the elastic pressure suit, he could sit, stand, and walk. He showed marked improvement in mood, increased physical activity, and weight gain. He was gradually able to

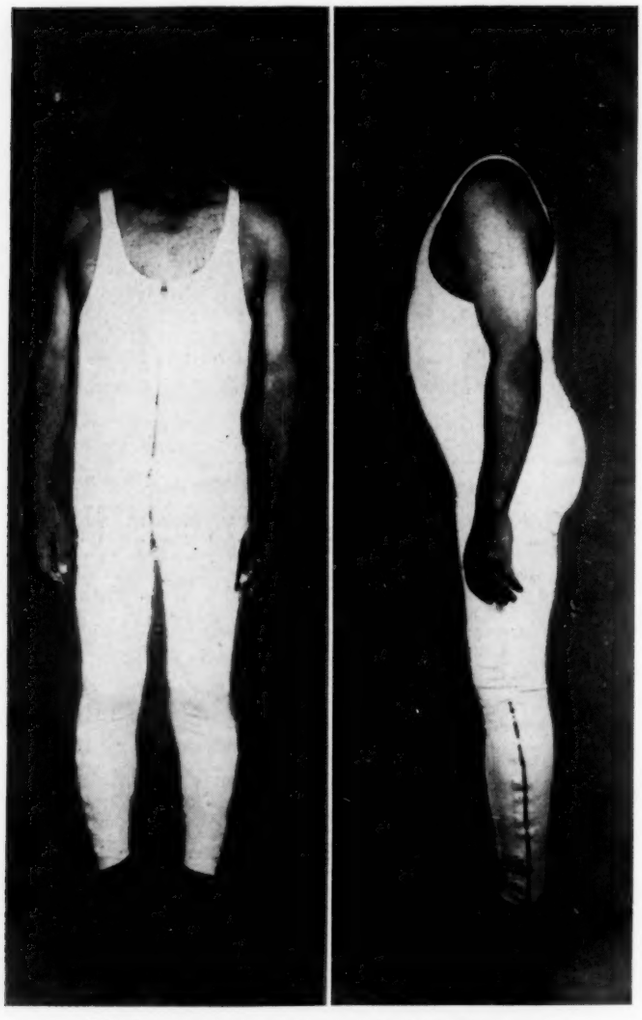

Fig. 1.—A patient wearing the elastic pressure suit.

resume part-time work as a business executive. After this marked improvement he found he had to use the suit less frequently and now uses it only when anticipating long periods of standing or during hot weather. A. M., a 46 year-old housewife, was restricted to a bed and chair existence for two years because of postoperative postural hypotension. With the use of the elastic pressure suit, the patient was able ultimately to return to limited daily activity, doing light housework and preparing the family meals. These two examples illustrate the use of the suit as a means for rehabilitation and suggest its effectiveness in making patients ambulatory who have postural hypotension that is disabling but that may gradually improve.

Two of the patients (E. H. and C. W.) died of their associated illnesses shortly after the study. They had used the suit for only short periods at home. In these patients symptoms of postural hypotension and syncope were lessened, although the individuals did not return to normal activity.

In order to elucidate the means by which the counterpressure garment opposes the postural fall in blood pressure, more detailed circulatory studies were carried out in four patients. The relevant data are presented in table 3. During a tilt in the unprotected state all four patients showed a marked fall in arterial pressure and an abnormal decrease in cardiac output. The calculated resistance changed relatively little. These are the usual findings in severe orthostatic hypotension. The systemic arterioles do not constrict effectively in response to a fall

TABLE 3.—*Effect of Tilt on Cardiac Output and Arterial Pressure of Four Patients*

Date	Patient	Condition	Mean Arterial Pressure, Mm. Hg	Cardiac Index, Liters/Min./Sq. Meter Body Surface	"Calculated Resistance," Mean Arterial Pressure / Cardiac Index
12/16/52	M. B.	Supine	93	3.3	28
		35 degrees without suit	48	1.7	28
		35 degrees with suit	79	2.1	38
12/15/54	J. S.	Supine	86	3.4	25
		55 degrees without suit	45	1.4	33
		55 degrees with suit	64	1.6	40
3/25/54	E. H.*	Supine	96	3.6	27
		60 degrees without suit	72	2.4	30
		60 degrees with suit	81	3.5	24
2/10/54	L. M.*	Supine	87	2.7	32
		60 degrees without suit	57	1.9	30
		60 degrees with suit	71	1.9	37

* A knit suit was used in this study.

in blood pressure,[1b] and this fall is often intensified by an abnormally great postural decrease in cardiac output.[2] In these four patients the postural fall in blood pressure was partially prevented by the use of the suit. The suit appears to have increased both cardiac output and peripheral resistance, although the effect varied from patient to patient. It appears likely that counterpressure may act by preventing undue dilatation of vessels under large hydrostatic pressures when the patient is in the erect position. Preventing arteriolar dilatation will support peripheral resistance, and preventing venous dilatation will promote return of blood to the heart. The

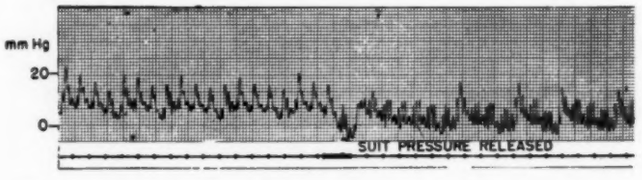

Fig. 2.—An example of the fall in pulmonary arterial pressure observed with release of pressure in the air-filled suit while the patient was tilted.

contribution of the suit in promoting venous return to the heart appears to be demonstrated by the experiment of abruptly releasing suit pressure when the patient is tilted. As shown in figure 2, there is a rapid fall in pulmonary arterial pressure. We interpret this as resulting from an abrupt decrease in right ventricular output

secondary to decrease in venous return. Contrariwise, when the air suit is inflated, there is a rise in both right atrial and pulmonary arterial pressures.

Summary

A usable type of tailored elastic pressure garment has proved effective in six patients and of practical value in four of these in preventing symptoms of orthostatic hypotension. The results confirm previous findings that counterpressure applied to the lower half of the body will alleviate postural hypotension. The present device appears to be more effective and practical than mechanical means that have been described before.

The suit has been a significant help in the rehabilitation of patients with severe postural hypotension. In cases in which postural hypotension might normally be expected to improve, as after sympathectomy, use of the suit may initiate and hasten the return of vasomotor tone. Counterpressure seems to be effective by preventing dilatation of both arterioles and veins by hydrostatic pressure. Supporting the arterioles helps to maintain peripheral resistance, and supporting the veins helps to maintain venous return and cardiac output.

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COMPLETE EXTIRPATION OF THORACIC DUCT

USE IN MANAGEMENT OF PRIMARY BENIGN TUMOR PRODUCING SPONTANEOUS CHYLOTHORAX

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• A patient whose symptoms had suggested the possibility of chronic appendicitis was found to have a chylothorax on the right side. Open thoracotomy revealed a tumor, cylindrical in form, involving the entire thoracic duct. The tumor was removed, with the duct contained in it, and the normal duct tissue at either end was ligated.

Suggestions of interstitial edema in the upper abdominal area appeared after the operation but disappeared in about five days. In all other respects the patient did exceedingly well and is still well two years after the operation.

The tumor was found to be a lymphangioma of the thoracic duct. This experience establishes the fact that the main thoracic duct can be ligated with impunity and that extensive portions of it can be excised without endangering the patient's life.

Case reports of traumatic chylothorax are not uncommonly encountered in the literature.[1] The types of trauma responsible for this disorder have included hyperextension injuries of the spine, penetrating wounds of the chest, fractures of the ribs and vertebrae, and accidental lacerations of the thoracic duct occurring in the course of surgical procedures. Other causes include forms of indirect trauma, such as severe coughing spells, blast injuries, convulsions, or injuries to infants resulting from overrigorous attempts at resuscitation during birth.[2] Chylothorax of nontraumatic origin is certainly less common and occurs usually in association with metastatic malignant disease with invasion of the thoracic duct or the superior vena cava and its branches.[3] Such metastatic involvement is encountered most frequently in cases of primary carcinoma of the stomach or neoplasms of the lymphoblastoma group. Tuberculosis of the mediastinal lymph gland, retracting tuberculous lesions of the lung, or tuberculous paravertebral abscesses have also been reported as causes of nontraumatic chylothorax.

Chylothorax regardless of cause is a serious occurrence, the mortality rate having been reported as high as 50% by many authors. Operative leakage is attended with an estimated 10% mortality rate. Surgical intervention, such as ligation or attempts at repair of the severed duct, produces a much higher mortality rate, sometimes even as much as 100% according to a report by Dorsey and Morris [4] in 1942. This is probably an abnormally high figure, as the management of chylothorax was mainly a subject of academic interest until Lampson,[5] in 1946, showed that the condition could be cured by ligation of the thoracic duct in the lower chest.

I should like to report briefly a case of spontaneous chylothorax that is unusual from several aspects. As nearly as can be determined, this is the first proved case of primary benign tumor of the thoracic duct to be treated in the manner to be described.

Report of a Case

A 37-year-old white woman was admitted to the hospital because of complaints of pain and tightness in the right lower quadrant of the abdomen. The admitting diagnosis was possible chronic appendicitis. Physical examination revealed some tenderness in the right lower quadrant on deep palpation but none of

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Dr. Walter C. Vester, Cincinnati, gave permission to publish this case report.

the classic findings of acute or chronic inflammation of the appendix. The breath sounds were diminished and the percussion note impaired over the lower aspect of the right side of the chest. No symptoms had been elicited referable to the chest. An x-ray of the chest made on May 8, 1953, showed

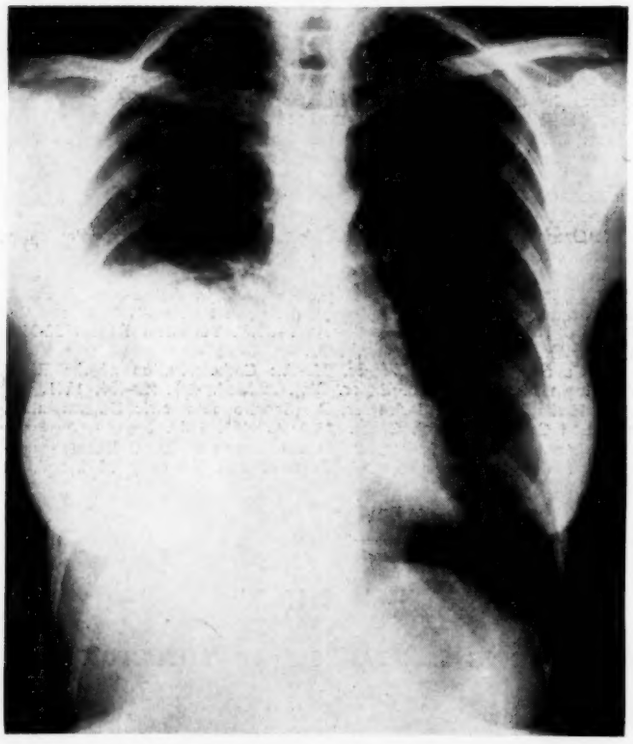

Fig. 1.—Posteroanterior projection roentgenogram of chest showing chylothorax.

fluid in the right lower thorax (fig. 1). Thoracentesis, May 12, yielded 1,000 cc. of creamy, tan, odorless fluid, which had the consistency and appearance of whole milk and a specific gravity of 1.017. Microscopic examination revealed cells containing fine droplets, which stained bright orange with Sudan 3. Bacterio-

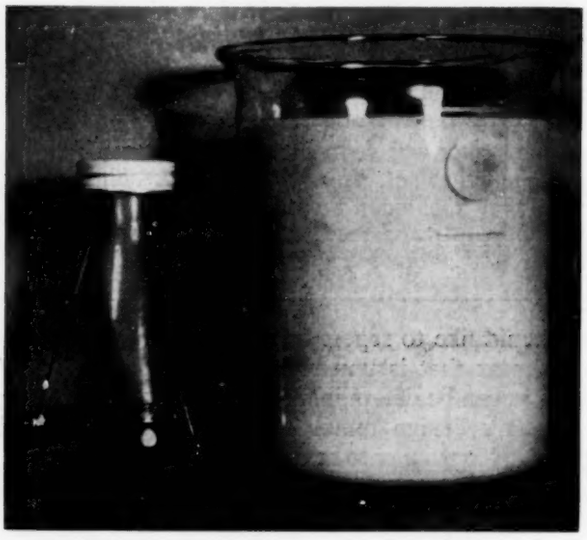

Fig. 2.—Identical quantities of chyle before and after alkalization and treatment with ether.

logical and cytological studies showed the fluid to be sterile, and no neoplastic cells were encountered. Alkalization and treatment with ether caused the color to clear and the volume to decrease, as is characteristic of chyle treated in this manner (fig. 2). The patient was treated by multiple thoracenteses and closed-tube thoracostomy drainage over a period of three weeks, with removal of approximately 7.5 liters of chylous fluid, without improvement.

Operation.—Because of constant recurrence of the chyle in the right pleural cavity, obvious deterioration of the patient, and fall in total blood protein level, open thoracotomy was decided upon. On June 15, with the patient in the left lateral prone position, the chest was entered through the bed of the eighth rib, which was subperiosteally resected. On entering the pleural cavity, a large quantity of chylous fluid was encountered and evacuated. There was a dense fibrinous peel over the surface of the lung and the parietal pleura of the chest wall. The lung was retracted out of the field, exposing the posterior mediastinum. There was moderate bulging of the lower portion of the mediastinum, and chyle could be seen leaking from a small aperture in the midportion of the area of bulge. Incision was made in the mediastinum over the area where leakage was most profuse, and an additional quantity of chyle under pressure was evacuated. The mediastinal pleura was then opened widely, exposing a long, soft, elastic, cylinder-shaped tumor, 2 cm. in diameter, replacing the thoracic duct in the space between the azygos vein, posteriorly, and the aorta, medially (fig. 3). Chyle constantly leaked from several pinpoint openings in the lower portion of the tumor. As the dissection was continued, the

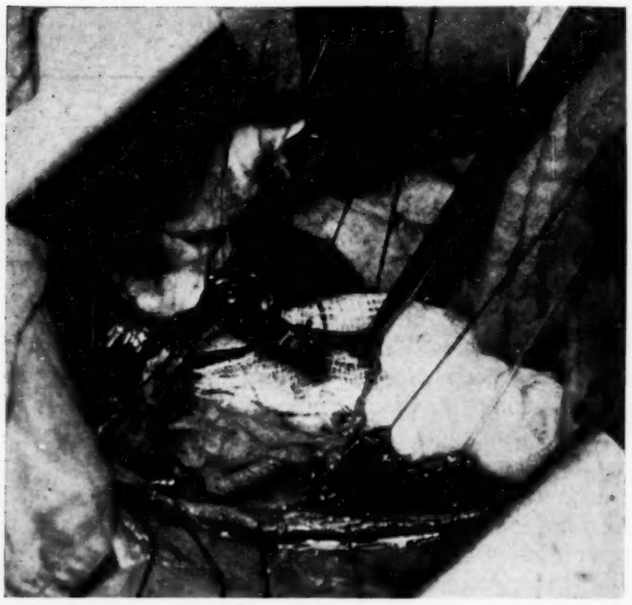

Fig. 3.—Tumor of thoracic duct held up by clamps and traction sutures

cylinder of tumor was seen to involve the entire thoracic portion of the duct, from the aortic hiatus to a point near the thoracic inlet beyond the level where the duct crosses the midline into the left side of the chest. It was obvious that removal of the entire thoracic duct would be necessary. The duct containing the tumor, therefore, was mobilized by freeing it from the esophagus and aorta, posteriorly and medially, and the azygos vein, laterally, down to the aortic hiatus. At this point the thoracic duct was doubly ligated and divided. Proximally the dissection was carried beneath the transverse crossing of the azygos vein, which was also ligated and divided. It was necessary to extend the dissection across the midline beneath the pleura into the opposite side of the chest up to the point where the thoracic duct enters the angle of junction of the left internal jugular and subclavian veins. Normal duct was encountered at this point, doubly ligated, and divided. The entire thoracic duct containing tumor was then removed from the chest. The mediastinal pleural edges were approximated loosely with interrupted medium nonabsorbable surgical (silk) sutures, and the lung was reexpanded. Drainage was established with an intercostal catheter connected to a water-seal bottle. The chest wall was closed in the usual manner with interrupted sutures of medium and fine cotton.

After operation the patient did exceedingly well, being ambulatory by her second postoperative day. The intercostal tube was removed on the day following operation, at which time roentgenograms of the chest showed the lung to remain completely expanded, with no recurrence of fluid. The patient was discharged home on her 11th postoperative day and has continued to do well up to the present time, approximately two years since the operation. During the first five postoperative days she did have some feeling of fulness in the upper abdomen, and on palpation the abdominal wall had a "doughy" consistency. This very probably was due to interstitial edema, which gradually cleared with increasing development of the collateral lymphatic circulation. After the first five days the feeling of fulness and the "doughy" consistency of the abdomen were no longer present. Pain in the lower abdomen, which was the presenting complaint on admission, most probably resulted from diaphragmatic pleurisy on the right incident to the chylothorax.

Laboratory Studies.—The red blood cell count on admission was 4,350,000 per cubic millimeter. The white blood cell count was 7,000 per cubic millimeter. The hemoglobin level was

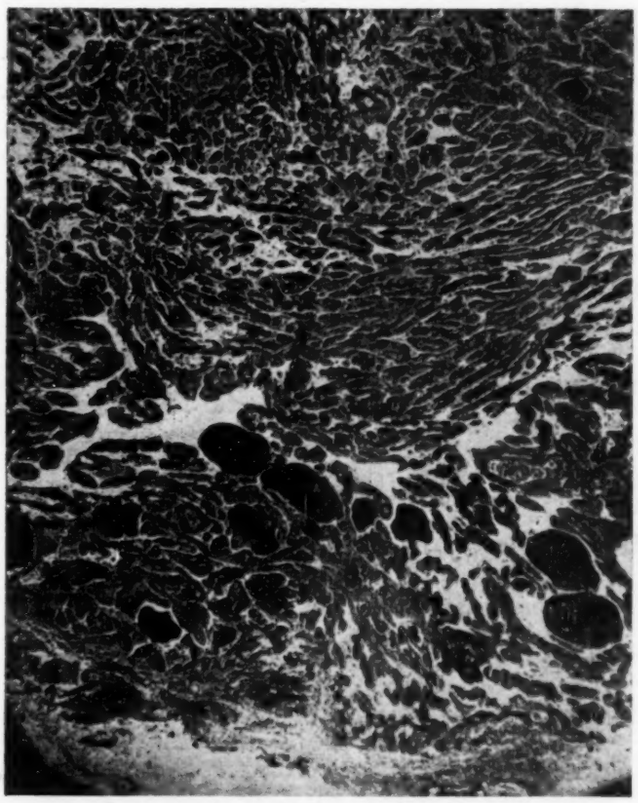

Fig. 4.—Photomicrograph of thoracic duct tumor showing numerous networks of lymph channels and focal collections of lymphocytes.

12.5 gm. per 100 cc. The differential count showed 19% lymphocytes, 75% segmented cells, and 6% monocytes. The total blood protein level on June 9, approximately one month after admission to the hospital and six days before open thoracotomy, was 6.7 gm. per 100 cc. The differential count on the day after surgery showed a drop of the lymphocytes to 7%. A repeat differential count on June 23, eight days after removal of the tumor and ligation of the duct, showed a rise in the number of lymphocytes from 7 to 19%.

Pathology.—The specimen consisted of 13 gm. of soft, grayish-white, spongy, cylinder-shaped material, 2 cm. in diameter. No normal thoracic duct could be recognized. Microscopically, the tumor presented the characteristic picture of a benign lymphangioma with numerous networks of irregular endothelial-lined channels containing lymph. Scattered throughout the tumor were focal accumulations of lymphocytes. The process was thought to be a benign neoplasm arising in the thoracic duct (fig. 4). The final diagnosis was lymphangioma of the thoracic duct.

Comment

The fall in percentage of lymphocytes in the blood smears before and immediately after surgery, with subsequent rise after removal of the thoracic duct tumor, suggested that an adequate collateral circulation was present and functioning. In the past it has been observed that following the rupture or ligation of the thoracic duct there is a striking drop in the number of lymphocytes and eosinophils in the circulating blood. As the lymphocytes are known to be carried through the thoracic duct to the blood stream, changes in the number of lymphocytes in the differential count can be used as a criterion for estimating the presence or absence of adequate lymph flow through collateral channels.

Although an excellent report on the establishment of collateral circulation following ligation of the thoracic duct was presented by Lee,[6] in 1922, it is interesting to see the series of complicated technical procedures that have been suggested in the literature for end-to-end anastomosis or implantation of cut ends of the thoracic duct into a vein in the years that followed, up to the time that Lampson [5] first successfully ligated a thoracic duct, in 1946. As late as 1949 the feasibility and good rationale of ligation of the thoracic duct by transpleural approach were discussed before the American Association for Thoracic Surgery in New Orleans by Meade and his associates.[7] Obviously, as demonstrated by Lee [6] in 1922, the thoracic duct can be ligated with impunity, for several reasons. After ligation the collateral lymph circulation is established through embryonic lymph channels, which normally do not function but which, in response to ligation, may be forced to enlarge and dilate. Also, after complete ligation, lymphaticovenous connections are found to exist between the thoracic duct and the azygos and intercostal veins. This is understandable when one recalls that the lymphatics develop from discrete mesenchymal spaces that persist as lymph sacs with openings into veins. The embryonic thoracic ducts are bilateral and symmetrical and have numerous cross anastomoses.

In 1946 Swift and Neuhof [8] reported a case of cervicomediastinal lymphangioma with chylothorax. The case was that of a 32-year-old man who was admitted to the hospital after a seizure of severe coughing. He had a circumscribed swelling in the left supraclavicular area. During the course of the hospital stay a pleural effusion was demonstrated in the base of the left lung. Thoracentesis yielded 10 to 15 cc. of white, milky fluid, which was thought to represent chyle. The character of the pleural fluid was not definitely established by clinical tests. There was a rapid subsidence of the symptoms, until only the cervical swelling remained. Exploration of the left supraclavicular region on Feb. 28, 1944, revealed no chylous fluid. Deep behind the clavicle a diffuse fatty mass with occasional vesicles was encountered and partially removed for study. The subclavian vein and thoracic duct were not exposed. Microscopic examination revealed areas of cystic dilatation with surrounding areas of lymphoid tissue. The presence of a cervical mediastinal lymphangioma was "postulated" but cer-

tainly not proved. This is the only case report I have encountered that even remotely resembles the one presented here.

Several generalizations can be made about lymphangiomas.[9] They have a cavernous or cystic character and as a whole are apparently subject to infection, either in part or in their entirety. They may be located throughout the body and associated with lymphoid tissue, either superficial or deep. They are most frequently found in the neck, the mesentery of the intestine, or the pelvis. Infections, when they occur, are most frequently due to streptococci. As a result of infection, stasis with backpressure develops, giving rise to distention of the tumor, which may then rupture. These observations could be offered as plausible explanations of the sequential development of clinical findings in the case that is reported here.

Summary and Conclusions

Surgical experience with excision of benign tumor of the thoracic duct producing spontaneous chylothorax establishes the fact that not only can the main thoracic duct be ligated with impunity but extensive portions of the mediastinal thoracic duct can be excised without endangering the patient's life. As nearly as can be determined, this is the first authenticated case of a true benign tumor of the mediastinal thoracic duct to be reported. From a review of the literature, this appears to be the first record of successful excision of extensive portions of the thoracic duct for any cause.

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CLINICAL IMPLICATIONS OF ERRORS IN ELECTROCARDIOGRAPHIC INTERPRETATION

HEART DISEASE OF ELECTROCARDIOGRAPHIC ORIGIN

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• Undue reliance on the electrocardiogram has created many problems in the diagnosis and management of heart disease. Subjective cardiac symptoms are frequently occasioned or intensified by the physician's unwarranted diagnosis of heart disease on the basis of some poorly understood or misinterpreted electrocardiographic aberrations. It is estimated that an average physician caring for cardiac patients sees from 10 to 25, and perhaps more, such cases of heart disease of electrocardiographic origin per year. The two most important symptoms of this disease are anxiety and chest pain.

Departure from the assumed normal, especially of the S-T segment and the T wave, does not always mean abnormality of the myocardium. Severe myocardial abnormality is sometimes present without significant electrocardiographic abnormality. Diffuse changes in the deeper layers of the myocardium sometimes fail to alter the electrocardiogram, while relatively insignificant lesions in the superficial layer sometimes alter it markedly. The most reliable guide in the diagnosis and management of heart disease is the patient's clinical state.

Virtually every new clinical sign or diagnostic laboratory procedure must undergo a period of evaluation before its true merits are determined. A glance at the history of medicine reveals that, in this stage of evaluation, the enthusiasm and faith of the clinician toward the sign or the test waxes and wanes periodically. In the most typical sequence of events, a period of initial popularity is followed by one of skepticism and rejection. It may be years or even decades before a given test assumes its proper place.

In the field of cardiology, similar trends have been prevalent. For example, after considerable knowledge was accumulated on the genesis of cardiac murmurs through the pioneer work of Laënnec and Bouillaud and the experimental observations of James Hope and others, systolic murmurs were regarded as indicative of heart disease. The degree of loudness of the murmur was often thought to represent the severity of the heart disease. The trend changed some three-quarters of a century later, after the studies of Sir Thomas Lewis, Henry Christian, and many others emphasized that systolic murmurs occur in normal as well as diseased hearts. Another example occurred in the early years of the 20th century, when patients with cardiac arrhythmias, such as sinus arrhythmia,

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dropped beats, and paroxysmal tachycardia, were assigned poor prognosis. Children with such arrhythmias were often confined to bed. Later the monumental work of James MacKenzie elucidated the harmlessness of such arrhythmias in a large majority of cases.

Now, we are witnessing a similar evolution in the use of the electrocardiogram. It is currently enjoying remarkable popularity. However, too many physicians expect an electrocardiographic tracing to tell them whether heart disease is present. Not uncommonly, the physician may rely almost entirely on the electrocardiogram for the diagnosis of heart disease, and, in so doing, underestimate the value of other important clinical data.

This undue reliance has created many problems in the diagnosis and management of heart disease. On one hand, the physician may hesitate to make the diagnosis of myocardial infarction in the face of overwhelming clinical evidence, simply because the electrocardiogram fails to show classic changes of myocardial infarction. On the other hand, the extreme awareness of coronary disease on the part of patients and physicians and the liberal use of the electrocardiographic machine for the clinical screening of heart disease are conducive to erroneous diagnoses of coronary disease in healthy individuals. Frank Wilson [1] was acutely aware of the harm rendered by incompetent and overzealous interpretation of such benign electrocardiographic changes and spoke of "miseries caused by the electrocardiogram."

With the increasing availability of electrocardiographic apparatus and the use of strategically well-located lead positions on all types of patients, probably more innocent electrocardiographic abnormalities will be discovered and, consequently, more healthy individuals made invalid. For the foregoing medical and socioeconomic reasons, we believe that a scrutiny of this problem is timely.

It is well to recall the words of Sir William Osler,[2] who said in 1894,"Not to receive the positive information they seek is often a great disappointment to both doctor and patient, but we must remember that there are—changing slightly Sir Thomas Browne's phraseology—cases indissoluble in physic and a diagnosis is not possible in every instance." Due to the paucity of knowledge concerning the genesis of the electrocardiographic components and to uncertainties involving the range of the normal, it is only natural that electrocardiographic misinterpretations have occurred. It is hoped that a review of facts relative to such errors will aid in reducing future errors to a minimum.

This study is primarily concerned with the possible consequences of an erroneous or overzealous diagnosis of heart disease on the basis of electrocardiographic alterations that are not necessarily diagnostic of heart disease. The symptom complex that develops under such circumstances is not a disease in the true sense of the word. However, for the purpose of convenience and emphasis, it is presented as a disease entity under the term "heart disease of electrocardiographic origin."

Symptom Complex

Definition.—Heart disease of electrocardiographic origin is a symptom complex in which subjective cardiac symptoms are occasioned or intensified by the physician's unwarranted diagnosis of heart disease on the basis of some poorly understood or misinterpreted electrocardiographic aberrations.

Etiology.—Many factors may contribute to the development of subjective cardiac symptoms in patients both with and without organic heart disease. In the absence of heart disease, probably the most important single factor is the erroneous interpretation of some benign electrocardiographic changes discovered on routine examination or because of symptoms with doubtful relation to the heart. This course of events occurs more frequently in individuals beyond the age of 40 years, due partly to the fact that physicians are prone to think of coronary artery disease in this age group and partly to the awareness of these individuals of the high incidence of heart disease.

Other factors that may influence the development of symptoms include the increasing availability of the electrocardiogram, the increased number of lay publications on heart disease, the high incidence of chest pain often unrelated to heart disease, and the lack of adequate interchange of information between the clinician and the electrocardiographic interpreter in those cases in which the electrocardiogram is interpreted by an individual other than the attending physician.

Incidence.—It is believed that the incidence of heart disease of electrocardiographic origin is on the increase. Currently, it is estimated, on the basis of correspondence with internists and cardiologists, that an average physician caring for cardiac patients sees from 10 to 25, and perhaps more, cases of heart disease of electrocardiographic origin per year.

Symptomatology.—The subjective symptoms of heart disease and particularly chest pain in (1) persons with certain electrocardiographic changes in whom no organic heart disease can be proved by the most careful history and clinical examination or (2) patients with organic heart disease, and especially old myocardial infarction, in whom the symptoms are often out of proportion to the degree of anatomic changes may be regarded as possibly functional in nature. In the first category, recognition of the nature of these symptoms is possible only by maintaining a high index of suspicion and by obtaining a scrupulous history. In those patients with organic heart disease, follow-up studies reveal that, while symptoms are persistent and progressive and unresponsive to the usual therapy, the concomitant organic heart disease is quiescent and of insufficient severity to cause symptoms. It cannot be overemphasized that persistence of chest pain or S-T segment and T-wave changes in patients with known coronary artery disease does not signify categorically that myocardial ischemia is present.

Symptoms may vary among patients and depend largely on the circumstances that precede their onset. Many individuals are influenced by illness or death due to heart disease of members of their families or friends and by articles in the lay press concerning heart disease. Anxiety and chest pain are common. "Weak spells" or fainting tendencies and palpitation are often reported.

Anxiety.—In some cases, the history reveals the presence of anxiety neurosis before the attention is focused on the heart; in others, it results from the discovery of some minor changes in the electrocardiogram. In the latter case, diagnosis of heart disease means to many patients the beginning of a progressive disability terminating in death. The marked anxiety and heart-consciousness that often ensues is a true iatrogenic phenomenon and therefore usually preventable by proper approach. Anxiety neurosis may appear in patients who suffer their first attack of myocardial infarction. The discovery of myocardial infarction in a person prone to anxiety will lead to the same chain of events as does the erroneous diagnosis of heart attack. It is the duty of the physician, therefore, to attempt to separate the symptoms due to coronary artery disease from those occasioned by the resultant anxiety. Not uncommonly, a patient with an authenticated history of myocardial infarction makes a complete functional recovery, only to suffer the emotional consequences of his previous heart attack. Such a patient continues to complain of symptoms referable to the heart even though the heart is functionally normal. It may be difficult to differentiate with any certainty between these two entirely different processes.

Chest Pain.—Chest pain may constitute the presenting complaint in some patients, while in others it appears after an erroneous diagnosis of heart disease has been entertained. The pain is usually a dull, constant ache involving the anterior chest wall. It is usually more intense on the left side than on the right. The site of predilection in women is the area subjacent to the left breast. The pain may be aggravated by torsion of the body or hyperextension of the neck and arms and is often relieved by bending forward. It may be brought on by emotional upsets or appear to be related to exertion. Detailed questioning, however, may implicate a change in body position or an increased amplitude of respiratory excursion caused by anxiety rather than the magnitude of physical work. The patient is seldom awakened by pain. Glyceryl trinitrate is without effect or may exert a placebo type of effect that becomes manifest within 5 to 30 minutes, long after the pharmacological effects of glyceryl trinitrate have regressed.

Weak spells may occur at the height of anxiety and chest pain. Careful history-taking may reveal the presence of precipitating factors, such as emotional upheavals, arguments, and particularly hyperventilation. Palpitation is common. Blood pressure and pulse rate remain unchanged during these attacks.

Physical Examination.—Signs of anxiety and apprehension may be quite manifest in the patient's facies and his reactions to questions related to the heart. The most helpful physical sign is tenderness of the anterior chest wall to firm fingertip pressure. The tenderness is more pronounced in patients complaining of chest pain; however, it can be elicited in patients without this complaint. It may be moderate to exquisite in severity. Its site may be the soft tissues or the skeletal structures. This tenderness is often a persistent finding and not necessarily associated with subjective pain. Pressure on the chest wall may elicit pain identical to that from which the patient has been suffering. The heart is usually normal in size and sounds. No cardiac abnormality can be demonstrated by the use of all available methods, except in the previously mentioned patients with known cardiac lesions in whom the symptoms are often out of proportion to the organic disease.

Diagnosis

Diagnosis of heart disease of electrocardiographic origin is based on the presence of subjective symptoms of heart disease and particularly chest pain in association with certain electrocardiographic changes in persons in whom no organic heart disease can be proved by the most careful history and clinical examination. Recognition of the nature of these symptoms is possible only by maintaining a high index of suspicion for heart disease of electrocardiographic origin and by obtaining a scrupulous history with special reference to the situations that antedated the onset of the symptoms.

In contrast to the chest pain described above, that of angina pectoris occurs episodically and there are periods of freedom from symptoms between the seizures. It is usually retrosternal in location with radiation to the neck, left shoulder, and left arm. The effect of glyceryl trinitrate is prompt, reaching its peak within several seconds, when the sensation of facial flush reaches its height. When tenderness accompanies angina pectoris, it is often found in an area removed from the area of subjective pain.

The differentiation between the electrocardiographic changes of myocardial ischemia and those of noncardiac origin is essential. An intelligent answer must depend on a thorough knowledge of the electrocardiogram in health, with its wide range of variations as well as changes due to noncardiac factors.

The QRS complex of the electrocardiogram is a stable component. Its abnormalities reflect myocardial disease. The S-T segment and the T wave, on the other hand, are most unstable, ostensibly due to their dependence on certain as yet poorly understood dynamic biochemical reactions that take place after completion of myocardial activation. S-T segment changes and T-wave abnormalities do not necessarily indicate anatomic damage. It is possible that S-T segment and T-wave changes occur as commonly in the absence of heart disease as in its presence. Noncardiac factors capable of producing S-T segment and T-wave changes are too numerous to list. They include autonomic nervous imbalances caused by various drugs or emotional influences, various metabolic states, such as postprandial changes, and severe electrolyte disturbances. Finally, S-T segment and T-wave changes may occur in the absence of either demonstrable cardiac or extracardiac factors.

Electrocardiographic Changes as Variants of the Normal.—The following electrocardiographic changes are variants of normal findings.

QRS Complex: Individual variations in the form of QRS complex, on the basis of changes in the electrical position of the heart, were recognized and thoroughly studied by Wilson and his colleagues.[1]

S-T Segment Deviations: Moderate S-T segment elevation of up to 1.5 to 2 mm. is not an uncommon finding in the electrocardiograms of young healthy individuals. It is most pronounced in athletes and persons with tall bodies and narrow chests and is a persistent finding in such individuals. This type of S-T segment elevation is not associated with signs or symptoms of myocardial disease but is assumed to be due to premature repolarization of the subepicardial myocardium. It is of practical importance to recognize this entity. Acute pericarditis has been diagnosed on the basis of such S-T segment elevation, which after further study proved to be normal for the individual.

T-Wave Inversions: T-wave inversion occurs in subjects with perfectly normal hearts. Such T-wave inversion has also been the cause of many erroneous diagnoses and continues to be a problem in clinical electrocardiography. An interesting entity is the type of T-wave inversion that appears in a limited number of leads taken from the area of the chest that overlies the cardiac apex. This T-wave negativity, termed by Grant [3] "isolated T wave negativity," created a great deal of confusion in the interpretation of the electrocardiogram in the days when only one precordial lead was taken. Even with the more numerous precordial leads currently in use, this type of T-wave inversion continues to be a puzzle to the clinician. In certain individuals, the area of T-wave negativity is considerably larger and encompasses the entire left side of the chest leading to negative T waves in all the precordial leads and occasionally in the limb leads. We have had occasion to observe several patients in whom T waves have been consistently negative as long as 15 years, during which time there has been no evidence of heart disease.

Electrocardiographic Changes Due to Emotions and Other Noncardiac Factors.—Profound S-T segment and T-wave changes associated with noncardiac phenomena have been recognized for some time. In a very important paper, Mainzer and Krause [4] in 1939, and subsequently in 1940, reported S-T segment and T-wave changes resulting from the fear of impending operation. They introduced the term "fear electrocardiogram" and warned against making an erroneous diagnosis of heart disease on the basis of electrocardiographic changes. Since that time numerous reports have appeared in the literature emphasizing the frequency of S-T segment and T-wave aberrations in psychoneurotic and mentally disturbed individuals. Recognition of this fact is believed to be of the utmost importance in the interpretation of the electrocardiogram. To most patients, having an electrocardiogram taken is an exciting and often frightening experience, especially if it is the patient's first experience and if the patient is emotionally unstable. The first electrocardiogram may be no more reliable than the first blood pressure reading obtained in the physician's office. Just as it is mandatory to obtain repeated blood pressure readings and determine the so-called base line level, it is important to remember that the first electrocardiogram may differ from the "base line" electrocardiogram. In addition to the emotional influences just described, S-T segment and T-wave alterations may follow administration of a variety of drugs that affect the autonomic nervous system; namely, epinephrine,[5] tetraethylammonium (Etamon) chloride, and many others. Postprandial T-wave changes are important to recognize, for they may closely mimic T-wave changes of coronary disease.[6]

Treatment

The treatment of patients with functional symptoms may be conveniently divided into two components, the prophylactic and the curative.

Prophylactic Treatment. — Prophylactic treatment should be aimed at improving the manner in which the clinical and laboratory findings are discussed with the patient. The discovery of a benign electrocardiographic aberration is similar to the finding of a functional heart murmur or postural albuminuria. Patients must be informed of its presence and educated thoroughly as to the significance of such a finding, which is so often ineptly called "abnormal." Patients unaware of having such normal variations are likely to become frightened and confused when told by their insurance or employment agency's physician of their presence.

It is incumbent upon the electrocardiographer who interprets electrocardiograms to avoid conveying a false impression of heart disease to the clinician in interpreting benign changes. The most effective way, it is urged, is to add to the interpretation of borderline tracings the phrase "such changes may occur in normal hearts," typed in capital letters. Under such circumstances, the physician may rely upon his clinical judgment.

Curative Treatment.—Reassurance and persuasion are the mainstay of the curative treatment in these cases. The patient must be convinced that his heart is sound. This can be done by outlining to him a program of physical exercise and participation in outdoor activities and discontinuation of cardiac drugs that he may be taking unnecessarily. The result of such practice is often gratifying. Within a few days the patient usually feels new strength and stamina. Anxiety decreases, paving the way for ultimate eradication of the symptom complex. Psychotherapy and other comparable measures by a competent specialist may be needed if the emotional disturbance is deep-seated. In occasional cases, pain and tenderness of the chest wall require palliative measures. Here again, reassurance and the demonstration to the patient, by fingertip pressure on the chest wall, that the pain is superficial in location provide some relief. In more obstinate cases, administration of corticosteroids as described in a previous paper [7] may be utilized. This has value not only in relieving the discomfort but also in serving as a therapeutic test.

Experimental Observations

Doubtless every physician dealing with cardiac cases has observed the discrepancies between the electrocardiogram and the actual state of the myocardium and has experienced the difficulties inherent in making a reliable anatomicopathological diagnosis of heart disease on the basis of the electrocardiogram. This is reflected in almost every textbook of medicine and cardiology. However,

there has been no adequate physiological explanation for the discrepancies. In an attempt to shed some light on this problem, a series of experimental observations was made both in dogs and in human subjects. The manner of genesis of the normal electrocardiogram was investigated, and the theories on which most of the current diagnostic criteria are based were reexamined by different, newer approaches. A résumé of some of the findings that have direct bearing on the problem under discussion is given below.

First, all layers of the myocardium do not appear to behave similarly insofar as the genesis of the electrocardiographic complexes is concerned. The outer layers of the myocardium are found to be mainly responsible for the recorded electrocardiographic potentials, while the inner layers are shown to be relatively silent. QRS changes resulting from involvement of the outer layers are marked and often out of proportion to the extent of the myocardial damage, while there appear to be little or no QRS changes in infarctions confined to the "silent" subendocardial layers. The QRS component of the electrocardiogram may remain unchanged so long as the myocardial lesion has not involved the outer layers.[8] The rate of impulse transmission through the inner layers is considerably faster than through the outer layers. Similar observations have been reported with the use of unipolar leads by Durrer and co-workers [9] and Sodi-Pallares and associates.[10]

Second, in transmural injury, the magnitude of S-T segment elevation recorded from the inner layers is small compared to that from the outer layers. The predominance of the subepicardial layers in this regard has been shown previously by Kisch and co-workers.[11] Both S-T segment elevation and depression can be accounted for by alterations of varying intensity involving the outer myocardial layers. The S-T segment depression that apparently results from minor changes of the subepicardial layers has been termed "primary epicardial S-T depression." [12] Similar conclusions have been reached in the study of S-T segment displacement in humans.

Third, a significant observation made in animal experiments and corroborated by direct studies of the human heart is that profound T-wave changes may result from minor reversible alterations (such as biochemical or physical) of the outer myocardial layers and in the absence of any demonstrable anatomic damage to the myocardium.

Fourth, it should be emphasized that the primary function of the heart is to pump blood, the electrocardiogram being merely a by-product of this main function. Using high-speed motion pictures, taken simultaneously with direct-lead electrocardiograms from specific areas of myocardium, frame-by-frame measurements to fractions of a millimeter of cardiac contractions were made with a Vanguard motion analyzer. These studies often revealed a complete lack of relationship between myocardial contractility and the electrocardiographic complex. Contractions were observed not only in areas exhibiting normal R waves but also, in some cases, in areas yielding total loss of the R wave or coronary Q-S waves. Conversely, loss of contractile power was found in some areas yielding Q-S waves as well as in areas possessing normal R waves. These observations stress the fact that cardiac function, and therefore the clinical state of the patient, cannot be determined on the basis of the magnitude of the electrocardiographic changes.

Comment

The electrocardiogram is undoubtedly one of the most useful diagnostic tests ever devised. However, it suffers a number of shortcomings. One of the most important of these is the difficulty in establishing the normal range for various components of the electrocardiogram. Because of this inadequate knowledge our diagnostic criteria have been based largely on hypothesis rather than well-documented facts.

The range of normal for the amplitude and duration of various electrocardiographic components has been subject to considerable divergence of opinion. Various authors and textbooks propose different standards for normalcy. Attempts have been made by various investigators to delineate the range of the normal beyond which electrocardiograms could be considered definitely abnormal. However, most such attempts have met with difficulty due to pronounced overlapping of the normal and abnormal. Fenn, White, and co-workers and others [14] have stated that the borderline between the perfectly normal and the definitely abnormal is so wide that it is unlikely that a sharp line between them could ever be drawn and that one should not attempt to do so.

An unusual opportunity was provided during World War II to examine large numbers of young, healthy individuals and analyze their electrocardiograms.[14] It was astonishing to note that a large percentage of healthy individuals showed electrocardiographic abnormalities that had to be considered evidence of heart disease by any criteria available at that time.

The New York Heart Association committee on criteria, in its 1953 publication, proposed certain standards for normalcy. It was specified, however, that these criteria were not to be used to separate the normal heart from the abnormal heart. It is apparent from these and the preceding observations that (1) the normal range is probably much wider than has been suggested and (2) departure from the normal, especially of S-T segment and T wave, according to any criteria, may not necessarily denote anatomic abnormality of the myocardium. On the other hand, severe myocardial abnormality may be present without significant electrocardiographic abnormality.

What then is the appropriate course of action to be taken in the interpretation of an electrocardiogram? The logical answer is to use the electrocardiogram as an adjunct to the diagnostic armamentarium and for the support of the clinical diagnosis, as is true of other laboratory tests. The clinical impression must supersede the electrocardiographic interpretation. Should the electrocardiogram be given to a specialist for interpretation, he must be furnished with adequate information concerning the clinical history and the evolution of the patient's symptoms. Recognition of those electrocardiographic altera-

tions that do not denote any myocardial disease is possible only through adequate knowledge of the normal variations. Review of the previous tracings is one of the most essential prerequisites to an intelligent electrocardiographic interpretation, provided that all the tracings are taken under identical circumstances in relation to such factors as meals, emotional state, and body position. It should be borne in mind, however, that "fear changes" may alter any of the tracings. In fact, the last tracing may appear abnormal due to certain fear changes resulting from recent emergence of some vague complaints about the chest. Therefore, knowledge of the patient's emotions and his attitude toward heart disease is often indispensable for correct electrocardiographic diagnosis.

The chronological order in which the electrocardiographic changes of myocardial infarction appear is also of practical significance. It has been known for many years that electrocardiographic changes of infarction may lag, sometimes by several days, behind the clinical symptoms of acute myocardial infarction. Patients with clinically unequivocal acute myocardial infarction associated with characteristic laboratory evidence of myocardial necrosis may have normal tracings for several days only to exhibit, rather suddenly, infarction Q-R or Q-S waves. These electrocardiographic changes may occur during the recovery period after subsidence of the acute symptoms. Correct diagnosis therefore may be missed in the early and most important stage of evolution of the infarction. A possible explanation for this seeming paradox is that, in the early period of such infarcts, the lesion may be predominantly subendocardial (due to the latter's comparatively poor blood supply). The subepicardial component of the lesion at this stage is of lesser severity, hence not demonstrable electrocardiographically. Later, the superficial layers may undergo further change accompanied by characteristic electrocardiographic changes of infarction.

Finally, a few cases of myocardial infarction defy all diagnostic efforts. Both the clinical picture and the electrocardiogram remain equivocal. Management in such cases must depend entirely on the judgment of the physician.

Summary

A symptom complex, described under the term "heart disease of electrocardiographic origin," is characterized by subjective symptoms of heart disease and marked anxiety occasioned or intensified by an inaccurate interpretation of the electrocardiogram. Electrocardiographic misinterpretations have occurred in the past and will continue to occur in the future due to the paucity of knowledge concerning the genesis of the electrocardiographic components and to uncertainties involving the range of the normal.

The two most important symptoms of the disease are anxiety and chest pain. Tenderness on firm fingertip pressure over the anterior chest wall is the most significant finding on physical examination. A correct diagnosis depends on the physician's high index of suspicion of heart disease of electrocardiographic origin and his awareness of two facts: First, chest pain does not always represent heart disease; it occurs as frequently in patients with normal hearts as in patients with coronary heart disease. Second, S-T segment and T-wave changes do not invariably denote myocardial abnormality and may sometimes be caused by the patient's fear or apprehension. Treatment consists of prophylactic and therapeutic measures. The phrase "these changes may also occur in patients with normal hearts" should be added to the interpretation of the tracings with equivocal S-T segment and T-wave changes. Curative therapy consists chiefly of reassurance.

It has been shown experimentally that the deep myocardial layers are relatively silent insofar as the genesis of electrocardiographic potentials is concerned. While diffuse lesions of the deep layers may fail to alter the electrocardiogram, relatively insignificant lesions of the superficial layers may bring about pronounced electrocardiographic changes. While the electrocardiogram is one of the most useful diagnostic aids, its interpretation is often fraught with considerable uncertainty. For this reason the clinical state of the patient with symptoms referable to the heart remains the most reliable guide in diagnosis and management.

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CLINICAL NOTES

SERUM GLUTAMIC OXALACETIC AMINOPHERASE (TRANSAMINASE) DETERMINATIONS

VALUE IN THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN THE PRESENCE OF LEFT BUNDLE-BRANCH BLOCK

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At the present time, when confronted with the problem of chest pain that is considered to be cardiac in origin, the physician regards the electrocardiogram as the final test in deciding if acute myocardial infarction has occurred. Too often, when the clinical diagnosis is suspected, the early electrocardiograms may be interpreted as normal or, if abnormal, may lack the features usually considered diagnostic of recent myocardial injury. When this happens, the unsuspecting physician, reassured by the negative electrocardiographic report, may fail to obtain serial tracings or he may even begin to look elsewhere for a diagnosis.[1] In this way the patient may be denied adequate therapy, including complete rest and anticoagulants for his heart attack.

In addition to the fact that early electrocardiograms may not show evidence of recent myocardial injury, certain additional difficulties arise in the electrocardiographic diagnosis of recent myocardial infarction. These include the fact that a previous myocardial infarct may leave residual electrocardiographic scars that will neutralize changes characteristic of injury current. Another well-established difficulty in the electrocardiographic interpretation of recent myocardial infarction is its diagnosis in the presence of left bundle-branch block.[2]

Normally the interventricular septum is stimulated from left to right, but in the presence of left bundle-branch block the right side of the septum is activated first. For this reason a unipolar lead that faces the epicardial surface of the left ventricle will begin with an upward deflection even in the presence of the "window" effect created by a recent infarct. This production of an R wave rather than a Q wave, usually considered diagnostic of necrosis of myocardial tissue, will thus obscure an otherwise pathognomonic feature. Furthermore, left bundle-branch block will produce ST-T deviation opposite in direction to the main QRS deflection (depression in leads over the left ventricle) and myocardial injury will produce ST-T elevation. These effects balance each other and hence characteristic injury current is also lost when left bundle-branch block occurs with recent myocardial infarction. Although certain electrocardiographic features have been described that suggest myocardial infarction in association with left bundle-branch block, these may not appear. If a Q wave does appear in lead 1 or in leads taken over the left ventricle when left bundle-branch block is present, this should suggest myocardial infarction with involvement of the interventricular septum.

A simple chemical test to identify recent necrosis in the myocardium would seem highly desirable. Recently it was demonstrated that the enzyme, glutamic oxalacetic aminopherase (transaminase), occurs normally in all human serum in a concentration of approximately 8 to 40 units.[3] Because the concentration of this enzyme is particularly high in myocardial tissues, LaDue and his co-workers investigated the activity of this enzyme in recent myocardial infarction.[4] They reported that the enzyme level is increased 2 to 20 times and that this represents an accurate index of destruction of aminopherase-rich tissue,[5] in this case myocardium. Providing the determinations are begun early enough, when the problem of ascertaining the presence of myocardial damage arises, the enzyme levels of aminopherase can be very helpful in diagnosis. The following case reports will demonstrate the value of this maneuver when the electrocardiographic diagnosis of recent myocardial infarction was in doubt because of the presence of left bundle-branch block.

Report of Cases

CASE 1.—A 60-year-old female first became ill about a month previous to her hospital admission on Sept. 6, 1955. At that time she was seized with sudden and severe epigastric distress, which was spontaneous in origin. Her pain radiated toward the sternum and into both arms. She also admitted to considerable dyspnea and sweating during the attack. A physician was called who gave her an injection for relief of pain, but she refused to be hospitalized. After this original episode she continued to be mildly symptomatic with angina but remained ambulant until the night before admission. At this time she had a similar but more severe episode and consented to hospitalization. The systemic review revealed no history of any significance, and she firmly denied all gastrointestinal symptoms, including any food intolerance, stating that she "could eat everything."

The medical history revealed that she was a diabetic, but she admitted that she did not watch her diet and took no insulin. The diabetes was discovered on routine urinalysis three years previously, when she had had an operation for an ovarian tumor. The only other episode in her medical history was a fractured femur about 20 years before. One hour after hospital admission the patient went into profound shock with marked dyspnea and cyanosis. She had severe epigastric pain, and her skin was cold and clammy. Pupils were round and equal and reacted to light and accommodation. Eyeground examination revealed a normal fundus. The thyroid gland was palpable but not nodular. Blood pressure was 100/50 mm. Hg. Heart rate was 120 per minute with a gallop rhythm; A_2 was greater than P_2; and there were crepitant rales at the left base. Abdominal examination revealed no enlargement of liver, spleen, or kidneys, and there was a lower abdominal scar from a previous operation. There was a 1+ pitting edema of the ankles. Tendon reflexes were equal and reactive.

On admission her blood sugar level was 200 mg. per 100 cc.; nonprotein nitrogen level, 35 mg. per 100 cc.; and the serum amylase level, 100 units per 100 cc. Urinalysis showed a 1+ test for sugar, was negative for albumin, and was negative microscopically. The sedimentation rate was 19 mm. per hour (corrected). Hemoglobin level was 11.5 gm. per 100 cc.; red blood cell count, 4 million per cubic millimeter; and white blood cell count, 7,050 per cubic millimeter, with normal differential. Liver function and electrolyte studies were normal. X-rays of gallbladder and gastrointestinal tract were normal. X-ray of the chest, which showed pulmonary congestion and

From the Montefiore Hospital Institute of Research.
Dr. Milton Bilder gave permission for use of case 2.

cardiac enlargement on admission (portable), was normal when the patient was discharged on Sept. 28, 1955, except for minimal cardiac enlargement.

Treatment consisted of therapy with levarterenol (Levophed) bitartrate, meperidine (Demerol) hydrochloride, oxygen, and anticoagulants and control of her diabetes. The patient continued to improve and was discharged from the hospital on Sept. 28, 1955. A review of her electrocardiograms (fig. 1) showed that the pattern of left bundle-branch block appeared in all tracings. In the tracings of Sept. 7 and 8, the diagnosis of recent anteroseptal myocardial infarction can be suspected because a Q wave

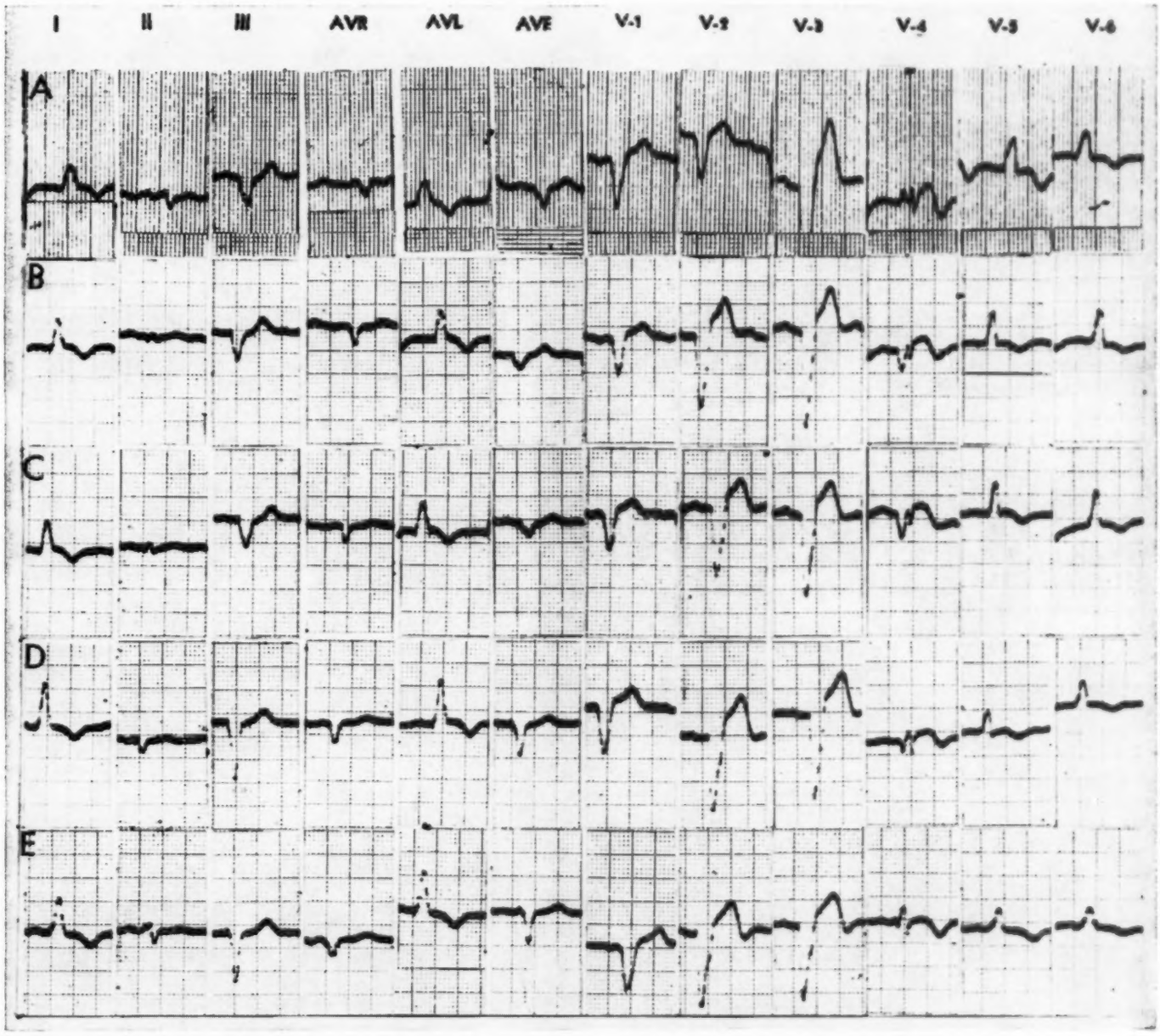

Fig. 1.—Electrocardiographic tracings for patient in case 1. *A*, Sept. 6, 1955; *B*, Sept. 7; *C*, Sept. 8; *D*, Sept. 12; *E*, Sept. 19.

appears in V_4 and there is coved elevation of the ST-T segment in this lead. In the tracing of Sept. 12, there is shouldering of the ST-T segment and the T wave is now diphasic in lead V_4. On Sept. 19 there is no longer a Q wave in V_4 and now the T wave is inverted, and in V_3 the T wave is diphasic. The serum glutamic oxalacetic aminopherase values were as follows: Sept. 6, 8 units; Sept. 7, 112 units; Sept. 8, 106 units; and Sept. 9, 84 units.

CASE 2.—A 75-year-old male was admitted to the hospital on Sept. 11, 1955, with a history of coronary artery disease for about 10 years. At that time he had experienced his first attack of acute myocardial infarction with good recovery. He had no further acute distress until about a week previous to his present hospitalization, when he suddenly became quite dyspneic, began to cough, and developed minimal ankle edema. On the morning of admission he developed acute and severe chest pain, which was not relieved by 150 mg. of meperidine. He was sent to the hospital by ambulance.

On physical examination he was quite cyanotic and orthopneic. Blood pressure was 90/60 mm. Hg. Head and neck showed no abnormalities. His chest was filled with rales and gargling sounds. Heart tones were distant, and there were frequent premature beats at a rate of 110 per minute. His liver was palpable to three fingers below the costal margin, and there was a 2+ pitting edema of both ankles. Neurological examination was normal.

On admission his blood sugar was 125 mg. per 100 cc.; nonprotein nitrogen level was 40 mg. per 100 cc.; and the icteric index was 5. The sedimentation rate was 11 mm. per hour (corrected); hemoglobin level, 11.5 gm. per 100 cc.; red blood cell count, 3,500,000 per cubic millimeter; and white blood cell count, 6,600 per cubic millimeter, and a normal differential. Urinalysis was negative for albumin and sugar. A roentgenogram of the chest taken on Sept. 12 (portable) revealed cardiac enlargement and congestion of the pulmonary vessels of both lung fields.

A review of the electrocardiograms (fig. 2) shows the presence of left bundle-branch block in all tracings. In the tracing of Sept. 11, there is the development of a tiny Q wave in the left ventricular leads that suggests recent myocardial infarction. A tiny Q wave is seen in lead 1 in most of the series and is best seen in the tracing taken on Sept. 15. The aminopherase determinations were as follows: Sept. 12, 120 units; Sept. 13, 46 units; Sept. 14, 60 units; and Sept. 15, 68 units. Unfortunately no further aminopherase determinations were run on this patient after Sept. 15. It is interesting to note that after the initial rise there was a fall to 46 units followed by a secondary rise, which probably was indicative of extension of the infarct.

aminopherase value obtained at the time of the second tracing. In the second case the electrocardiographic diagnosis of recent myocardial infarction was even less obvious, but again the elevated aminopherase values supplied good evidence that myocardial injury had taken place. Another interesting feature of this case was the fact that the aminopherase values showed a secondary rise after the initial decline. This might mean extension of the infarcted area and could be an important prognostic feature, a problem that we are presently pursuing

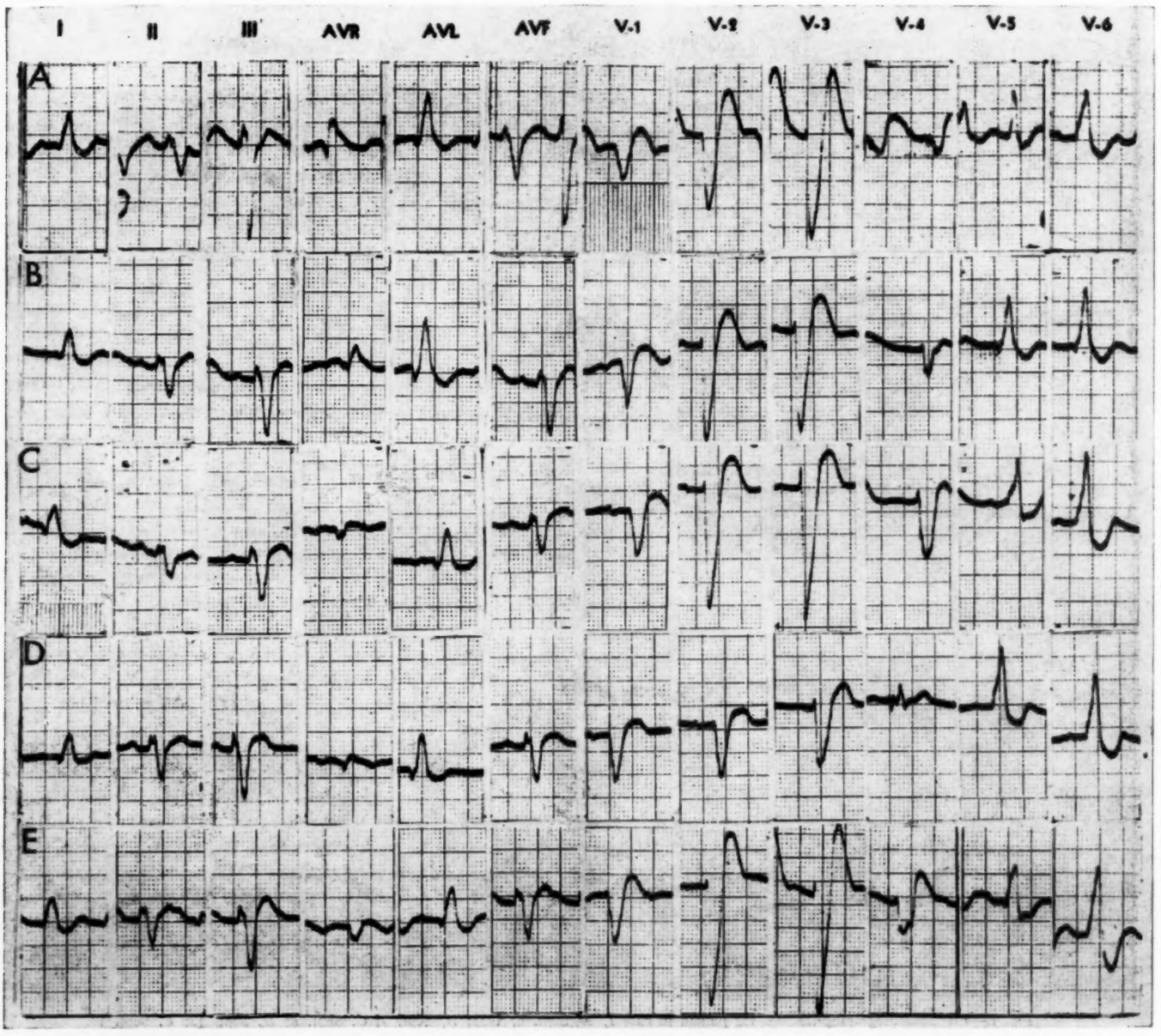

Fig. 2.—Electrocardiographic tracings for patient in case 2. *A*, Sept. 10, 1955; *B*, Sept. 11; *C*, Sept. 15; *D*, Sept. 20; *E*, Sept. 29.

Summary and Conclusions

The spectrophotometric analysis of serum glutamic oxalacetic aminopherase (transaminase) activity was used to clarify the diagnosis of recent myocardial infarction in the presence of left bundle-branch block. Our first case was complicated by diabetes mellitus and a high initial blood sugar value. Early electrocardiograms were not diagnostic of recent myocardial infarction, but the clinical impression was strongly supported by the elevated aminopherase value obtained at the time of the second tracing. In the second case the electrocardiographic diagnosis of recent myocardial infarction was even less obvious, but again the elevated aminopherase values supplied good evidence that myocardial injury had taken place. Another interesting feature of this case was the fact that the aminopherase values showed a secondary rise after the initial decline. This might mean extension of the infarcted area and could be an important prognostic feature, a problem that we are presently pursuing in our laboratory. Serum glutamic oxalacetic aminopherase determination is an aid in the diagnosis of recent myocardial infarction in the presence of left bundle-branch block.

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A NEW TYPE OF LOCALLY APPLIED STEREOTAXIC INSTRUMENT

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The development of subcortical surgery, with injections of chemical agents and radioisotopes into cystic brain tumors, and the treatment of intractable pain, involuntary movements, and tremor, by injecting specific nuclei, center around the satisfactory design and use of a human stereotaxic instrument. The idea of locating a needle tip in subcortical structures of the brains of cats and monkeys, with reference to a coordinate system, was first described by Horsley and Clarke.[1] Their coordinate system dealt with rectangular coordinates using the external canal of the ear, the orbit, and the midline of the skull as fixation and reference points. This is the coordinate system that has been most frequently used by designers of similar instruments for the human brain. Leksell's [2] instrument is an exception to this, in that it uses polar coordinates with an arc of a circle as the fixed frame. At present we have found description of 11 different human stereotaxic instruments in the literature beginning with that of Spiegel, Wycis, and co-workers.[3] It was our opinion that most of the instruments designed for human use have presented the following difficulties: 1. They were uncomfortable to the patient over a long period of time because of their means of application, often using the external auditory meatus and floor of the orbit as resting points for the supporting structures. 2. They were too cumbersome on the patient's head because of the large supporting frames, usually requiring that the patient be asleep and the head be supported mechanically. 3. They were difficult and time consuming in application in order to achieve the desired and necessary accuracy (within 1 to 2 mm. of the objective). 4. It was difficult to obtain the desired accuracy because of unsatisfactory fixation points (when external auditory canals, nose bridge, and orbital planes were used).

With these factors in mind we have designed a lightweight stereotaxic instrument (fig. 1) that attaches locally to any desired position on the skull and achieves the high degree of accuracy essential for this type of work. This instrument is constructed mainly of anodized aluminum with one part (needle-holder) made of a type of plastic that readily withstands sterilization. The entire instrument is sterilized by autoclaving. The total weight is 1.5 lb.

The instrument is fixed to the outer table of the skull by a circular aluminum ring with three small screws tapped into the outer table (fig. 1 *B*). The electrode holder then attaches by a knurled thumbscrew to the base or aluminum ring. Its position, referable to the midline and to the basal plane, is then controlled and fixed by a rubber-enclosed arm filled with Wood's metal and chain (fig. 1 *B*). After the holes are tapped in the external table of the skull, the aluminum ring and arm are immersed in boiling water, which causes the arm to become malleable. In this condition it is removed from

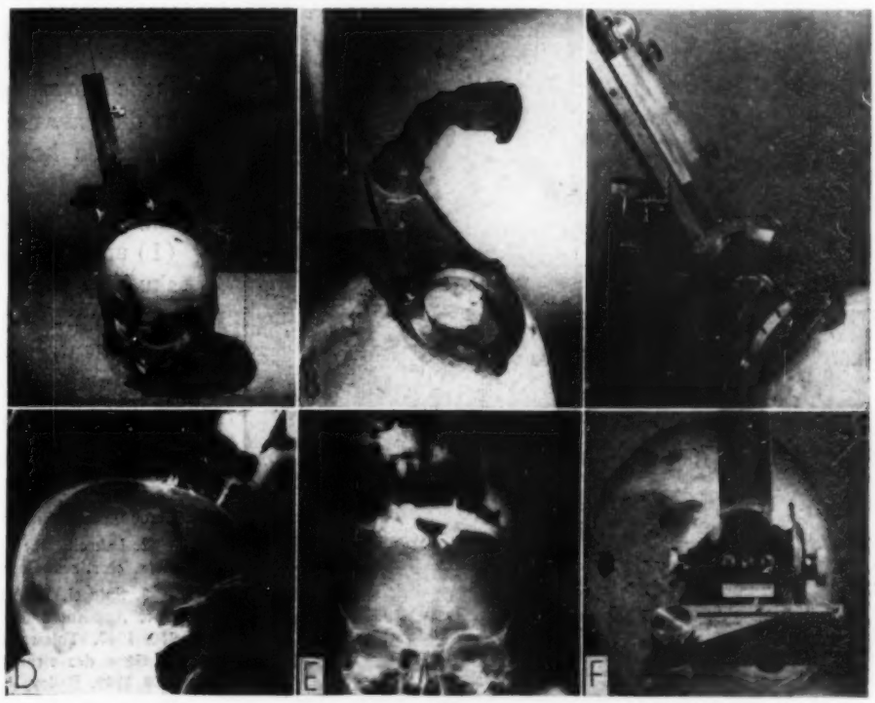

Fig. 1.—*A*, stereotaxic instrument attached to the right posterior part of the occiput. Note the 19-gauge needle in position along the electrode track. *B*, base, consisting of a circular aluminum ring, screwed on to the outer table of the skull. Arm filled with Wood's metal and enclosed in rubber tubing arises from the edge of the base. *C*, the sagittal angular plane of adjustment with vernier, set at right angles to the translation movement. There is a millimeter scale along geared electrode track. *D*, lateral roentgenogram of the patient's head with stereotaxic instrument attached. Metal clips are attached to the edge of the small scalp incision around base of instrument. *E*, anteroposterior roentgenogram of the patient's head with stereotaxic instrument in place. The needle projects down to the outer table of the skull and has not yet been inserted. *F*, posterior view of the attached instrument to show coronal plane of angular adjustment and the lateral translation movement.

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This study was aided in part by the Caroline W. Trimble Memorial Fund, Inc., and by a contract between the Office of Naval Research and the University of Pennsylvania. Reproduction in whole or in part is permitted for any purpose of the U. S. Government.

the water, screwed onto the skull, using 8-32 stainless steel screws, and the main electrode carrier affixed. The vernier on the sagittal angular scale is fixed parallel at right angles to the vernier, is fixed perpendicular to the basal plane (formed by a line through the base of the orbit, zygoma, and external auditory canal) (fig. 1*C*). to the midline, and the translation movement, which is The stereotaxic instrument is then held in this position until the Wood's metal has hardened (four to five seconds after removal from hot water). In this position and with the needle electrode properly aligned toward the desired structure, preliminary x-rays are made (fig. 1 *D* and *E*). Final adjustments are made, the electrode holder is removed, and a burr hole is made in the skull for electrode insertion. A small angular adjustment is present in the coronal plane that permits an angular approach up to 15 degrees to the midsagittal plane (fig. 1 *F*). This permits insertion into near midline structures through a burr hole at least 2 cm. from the midline, thus avoiding troublesome venous bleeding. The millimeter scale along the geared needle track permits the final measurement

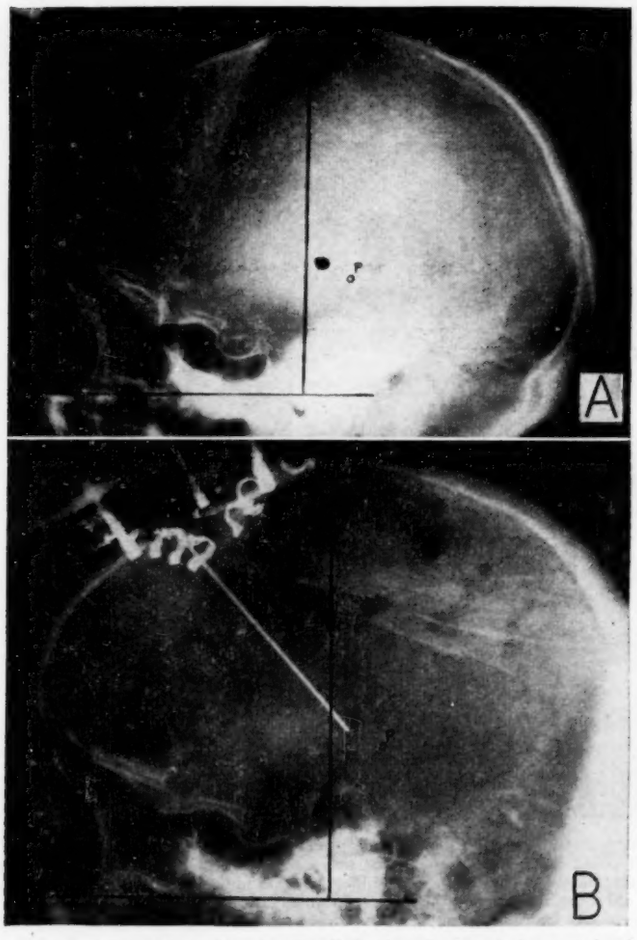

Fig. 2.—*A*, position of nucleus medialis dorsalis in relation to pineal gland (P), base line, and interaural line. *B*, needle in place in nucleus medialis dorsalis of left thalamus in same patient as in *A*.

for depth of electrode insertion, after this distance is plotted from the x-ray films (figs. 2 and 3). This instrument presents certain unique features of both polar and rectangular coordinates that we believe permit greater versatility and a greater sensitivity for final corrections of the needle electrode position.

Summary

A new lightweight stereotaxic instrument (weighing 1.5 lb.) for use in the brain of human beings is constructed mainly of anodized aluminum with a sterilizable plastic electrode holder. The instrument may be attached any place on the skull by means of three screws in the external table of the skull. The position of the electrode holder, referable to the basal and sagittal planes, is fixed by an arm filled with Wood's metal and chain. The reference planes of measurement include (1) an angular adjustment along the sagittal plane of the skull by means of a vernier; (2) a coronal plane of angular adjustment up to 15 degrees; (3) a translation movement, lateral from the midline; and (4) a vertical measurement along the electrode track.

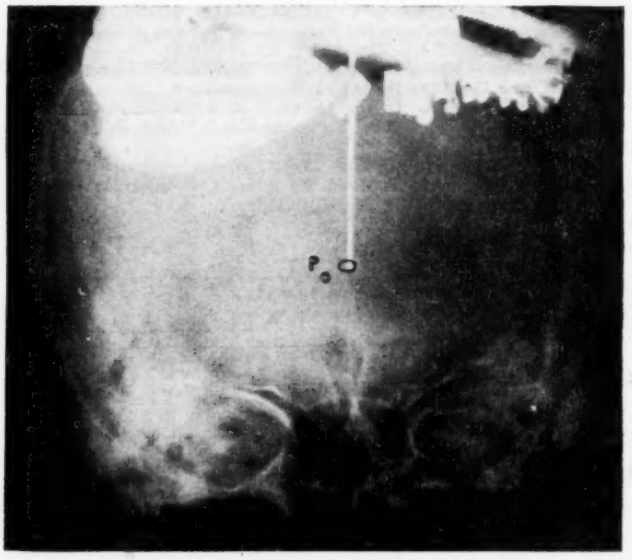

Fig. 3.—Anteroposterior view of same patient as in fig. 2, showing needle in place in nucleus medialis dorsalis of left thalamus. Nucleus was injected with 1 cc. of 95% alcohol for relief of intractable pain. Patient was relieved of pain and drug addiction without neurological deficit.

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COMPLEMENT FIXATION IN CAT SCRATCH DISEASE EMPLOYING LYGRANUM C. F. AS ANTIGEN

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Mollaret and others [1] employed Lygranum C. F. as an antigen against serums taken at various stages of cat scratch disease from 43 patients with clinically and skin test–proved disease and found a low complement-fixing titer in 20 (46.5%) (see table). They did not state the ages of their patients, nor did they record the results of tests on serums from any comparable group of normal individuals. They did, however, report finding an increased titer in serum from two patients in second bleedings. Serums drawn from each three to four weeks after the glands enlarged were negative but gave titers of 1:10 and 1:80 some weeks later. These authors deemed positive findings to have some diagnostic significance in cat scratch disease and to indicate that the disease belonged to the psittacosis-lymphogranuloma group of diseases. Lygranum C. F. is a commercial antigen prepared from venereal lymphogranuloma virus. The antigen gives complement fixation in trachoma, psittacosis, venereal lymphogranuloma, and several types of pneumonia but does not differentiate among them.

Kalter and others [2] reported Lygranum complement fixation in single bleedings taken late in the illness from 22 patients with cat scratch disease, with 12 positive (54.5%). Two of these patients whose serums yielded positive reactions in dilutions of 1:5 and 1:20 were bled about two weeks later; the second serums were positive in dilutions of 1:5 and 1:80 respectively. The ages and skin-test reactions were not stated, and results with serums from a comparable group of normal individuals were not reported. These authors chose to consider a positive reaction with serums in a dilution of 1:5 as significant, while we and Mollaret ignore this low reading. If the latter opinion had been applied, the percentage of positive reactions in the series under consideration would have been reduced to 31.8%.

From the National Microbiological Institute, National Institutes of Health (Dr. Armstrong and Mr. Turner), and the Department of Medicine, Georgetown University Medical School (Drs. Daniels and MacMurray).

At the National Institutes of Health one of us (H. C. T.) examined serums from 40 patients with clinically typical and skin test–proved cat scratch disease at stages during or after the attack, using a technique similar to that of Mollaret and his co-workers. (The titers recorded in our series were the highest dilutions showing a 4 + inhibition of hemolysis.) In 12 of these patients, varying in ages from 2 to 24 years, the serum of one, aged 10, gave a positive fixation reaction (8.3%), while among 23 patients 32 to 73 years of age there were 7 (30.4%) positive reactions (in patients aged 32, 34, 37, 38, 38, 40, and 47 years). There were five patients of unknown age whose serums all failed to fix complement (see table).

Gsell and others [3] report three patients who gave fixation titers of 1:10, 1:10, and 1:20 with a technique similar to Mollaret's. These three patients, 23, 27, and 44 years old, respectively, were from a group of nine patients proved by skin test to have the disease, six of whom, aged 5 to 15 years, were not tested.

Mollaret and his co-workers [1] feel that any complement-fixation reaction positive in a serum dilution greater than 1:5 has significance and indicates that such serums contain antibodies capable of combining with one or more antigenic components found in Lygranum. However, the assumption that such antibodies in cat scratch disease are caused by this infection needs further proof. In fact, the higher incidence of immunity in our series among older persons as compared to younger, all victims of cat scratch disease, suggests some source for the antibodies other than this ailment. Moreover, it is known that Lygranum will react with complement-fixing antibodies from a number of different diseases of man, an attack by any one of which could logically explain the presence of antibodies and readily account for the higher incidence of fixation found in serums from our older as compared to younger patients.

In order to elucidate this question, we examined, by the same technique, serums from 71 persons who had had no known attack of cat scratch disease and found 8 positive reactors (11.2%). There were 2 (5%) positive reactors among 40 of our controls, whose ages varied from 4 to 25 years, while among 31 persons from 32 to 68 years of age we found 6 (19.3%) whose serums fixed complement. One of these patients gave a history of having had psittacosis 25 years before. The source of the antibodies in the other seven controls is unknown.

Complement Fixation Results of Lygranum C. F. Antigen Serums from Patients Who Have Had Cat Scratch Disease and from Persons with No History of the Disease

Tests by	Antigen Employed	Source of Serums	Age of Donors, Yr.	Fixation Titers							No. Positive	No. Negative	Total Tested	Positive Reactions, %
				1:5	1:10	1:20	1:40	1:80	1:160	1:320				
Mollaret and others [1]	Lygranum	Patients who have had cat scratch disease	?	..	5	6	3	5	1	0	20	23	43	46.5
Kalter and others [2]	Lygranum	Patients who have had cat scratch disease	?	5*	1	2	2	1	1	0	12	10	22	54.5 (31.8)*
				1:8	1:16	1:32	1:64	1:128	1:256					
Armstrong and others	Lygranum	Patients who have had cat scratch disease	2-24	..	0	0	1	0	0	0	1	11	12	8.3
			32-73	..	1	1	3	2	0	0	7	16	23	30.4
			?	..	0	0	0	0	0	0	0	5	5	0
	Lygranum	Controls	4-25	..	1	1	0	0	0	0	2	38	40	5
			32-68	..	2	2	2	0	0	0	6	25	31	19.9

* Readings of positive in titers of 1:5 ignored by Mollaret and others and Armstrong and others.

To assume that their origin was cat scratch disease, however, would ignore other possible sources and lead to the necessary assumption that apparent cat scratch disease, or its inapparent but immunizing form, is more common than now realized. Debre and Job [4] in their extensive review of the literature found five possible cases of the latter type.

Summary

The presence of low-titered complement-fixing antibodies to Lygranum C. F. antigen in the serums of a minority of patients with classic cat scratch disease is confirmed by a series of tests done in patients known to have had the disease. The reaction, however, is also found in others, especially among older controls not affected with the disease and with no history of an attack. Likewise, among our actual cases, such low-titered reactions appear related more to the age of the patient than they do to the presence of cat scratch disease. In our opinion, the demonstration of a positive complement-fixing reaction to Lygranum C. F. antigen is without diagnostic value in the individual case of cat scratch disease and affords no convincing evidence that the disease belongs to the psittacosis-lymphogranuloma group of diseases.

1. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: La découverte du virus de la lymphoréticulose bénigne d'inoculation: caractérisation sérologique et immunologique, Presse méd. **59**: 681-682 (May 19) 1951.
2. Kalter, S. S.; Prier, J. E., and Prior, J. T.: Recent Studies on the Diagnosis of Cat Scratch Fever, Ann. Int. Med. **42**: 562-573 (March) 1955.
3. Gsell, O.; Forster, R., and Klaus, E.: Virus-Kratz Lymphadenitis (maladie des griffes de chat, lymphoreticulosis benigna), Schweiz. med. Wchnschr. **81**: 699 (July 21) 1951.
4. Debre, R., and Job, J. C.: La maladie des griffes de chat, Acta Pædiat. (supp. 96) **43**: 1-87, 1954.

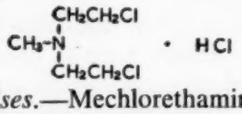
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary*.

Mechlorethamine Hydrochloride.—2,2′-Dichloro-N-methyldiethylamine hydrochloride. — Methyl-bis(beta-chloro-ethyl)amine hydrochloride.—The structural formula of mechlorethamine hydrochloride may be represented as follows:



Actions and Uses.—Mechlorethamine hydrochloride, a nitrogen mustard also known as HN_2, is a nitrogen analogue of sulfur mustard, the vesicant gas of World War I. The drug is highly toxic, both locally and systemically, and can produce a variety of actions, depending on the dosage administered. When administered intravenously to man or animals, the drug is rapidly removed from the blood stream and reacts quickly with the tissues. In experimental animals, lethal parenteral doses of mechlorethamine hydrochloride produce a powerful stimulation of the central nervous system and intermittent convulsions precede death, which usually results from respiratory failure. Progressive muscular paralysis follows subconvulsive doses. Minimum lethal doses administered to experimental animals produce a typical delayed death syndrome that consists of anorexia, weight loss, profuse vomiting, hemorrhagic enteritis with diarrhea, depression of hematopoiesis, and disturbances of electrolyte and water balance. There is no antidote; despite vigorous corrective therapy, death inevitably ensues, usually in 3 to 7 days. Like the parent sulfur mustard, mechlorethamine hydrochloride is a powerful vesicant; inhalation of dusts or vapor and contact with skin or mucous membranes produce severe local necrotic reactions.

The therapeutic use of mechlorethamine hydrochloride is based upon its cytotoxic and growth-inhibiting actions. Although it is cytotoxic for all cells, the compound has a special affinity for the intestinal and corneal epithelium, germinal tissues, the lymphatic and hematopoietic systems, and rapidly proliferating cells of certain neoplastic growths. In clinical use, bone marrow and lymphatic tissues are the only normal tissues significantly affected. In general, the mechanism of the cytotoxic action of the nitrogen mustards is at present imperfectly known; however, it is well established that compounds of this class inhibit cell division in the premitotic or resting phase. The striking similarity in toxic effects, biological action, and therapeutic results between nitrogen mustards and irradiation of the whole body with x-rays has resulted in the classification of the former as radiomimetic agents.

Mechlorethamine hydrochloride is useful for the palliative treatment of certain neoplastic diseases, particularly those of lymphoid and hematopoietic tissues. These include Hodgkin's disease, lymphosarcoma, certain types of chronic leukemia, lymphoblastomas of the skin, and mycosis fungoides. It is not intended as a substitute for accepted forms of radiation therapy, but rather as supplementary and complementary treatment in appropriate cases. Because of the toxicity and unpleasant side-effects that follow the administration of mechlorethamine hydrochloride, indiscriminate trial of this drug in patients with inoperable cancer or in the terminal stage of this disease is entirely unjustified.

Before therapy with mechlorethamine is initiated, an accurate histological diagnosis of the disease must be made and the hematological status of the patient determined. It is essential to understand the hazards to be encountered and the therapeutic effects to be expected. An adequate clinical history is important, and careful judgment must be exercised in the selection of patients. If the indication is not clear, the drug should not be used.

Mechlorethamine hydrochloride is usually most effective in certain generalized, but not terminal, neoplastic diseases. For localized involvement, x-ray therapy is generally the initial treatment of choice. The drug may palliate the disease in patients who have become refractory to radiation therapy, and it can be used in alternating courses with x-rays to control systemic symptoms; however, subsequent courses of nitrogen mustard therapy are usually not as effective as the preceding course.

In suitable cases of Hodgkin's disease, mechlorethamine hydrochloride may cause temporary remissions of varying duration. X-ray therapy should be employed in early and localized disease and the use of the drug reserved for widely disseminated lesions that are either refractory to radiation or are too widespread to be adequately treated by conventional radiation techniques or in cases with gross systemic symptomatology without localized lesions. The drug is also of value in producing temporary relief of pressure on the trachea and superior vena cava in patients with thoracic lesions. In such cases, mechlorethamine may be the treatment of choice, since it does not produce the local edema that usually follows radiation therapy.

In certain histological types of malignant lymphoma, mechlorethamine hydrochloride is useful after initial local x-ray therapy in the palliation of widely disseminated lesions. It has been most effective in appropriate cases of giant follicular lymphosarcoma; remissions lasting for months may be expected to occur. Although the drug is somewhat less effective in small cell or lymphocytic lymphosarcoma, its alternative employment with radiation will sometimes result in partial remission of variable duration. The drug is rarely effective in reticulum cell lymphosarcoma.

Although mechlorethamine hydrochloride has been widely employed for the palliative therapy of chronic granulocytic (myelogenous, myeloid) leukemia, other forms of therapy are currently considered superior for this purpose. These include x-ray, either as a total body spray or intensive local irradiation of the spleen, sodium radio-phosphate (P^{32}), and busulfan; however, many hematologists prefer to treat this disease with the sequential use of chemotherapeutic agents and radiation. In such a scheme, mechlorethamine hydrochloride is most useful in the early stage of the disease but is ineffective in terminal cases. Remissions, usually lasting 1 to 3 months, are characterized by a fall in the leukocyte count, an increase in the hemoglobin level, regression of enlarged lymph nodes and spleen, and general improvement.

Mechlorethamine hydrochloride has been used in patients with chronic lymphocytic (lymphatic, lymphoid) leukemia. The tendency of the drug to produce a greater destructive effect on the normal bone elements than on the leukemic lymphocytes has limited its usefulness. The drug is completely ineffective in the treatment of all types of acute leukemia.

In mycosis fungoides, mechlorethamine has been reported to produce relief of pruritus and regression of lesions in a significant number of patients with extensive skin involvement. Localized or early lesions should be treated by conventional x-ray therapy, and, if satisfactory improvement is not obtained, mechlorethamine may be given in the same manner as for Hodgkin's disease.

Bronchogenic carcinoma is the only epithelial tumor that responds significantly to therapy with mechlorethamine hydrochloride. The susceptibility of the tumor is largely influenced by its histological characteristics; anaplastic lesions are much more amenable to therapy than are the more differentiated tumors. When roentgenologic examination or exploratory thoracotomy reveals that the neoplasm is inoperable or when extensive metastases are present, the initial treatment of choice is generally x-ray therapy; however, mechlorethamine may be administered in cases not suitable for, or not responding to, x-ray therapy. Remissions include transient regression of lesions and resorption of pleural effusions in addition to alleviation of cough, dyspnea, hemoptysis, pain, and weakness. The remissions are of short duration, and subsequent courses of drug therapy are less effective. Mechlorethamine is indicated as the initial therapy only in superior vena cava (mediastinal) compression syndrome associated with inoperable bronchogenic carcinoma.

Because of the serious nature of its local and systemic toxic effects, the clinical use of mechlorethamine hydrochloride involves numerous immediate and delayed hazards and should be administered only to patients who are under close hospital supervision. Thrombosis and thrombophlebitis may result from direct contact of mechlorethamine with the intima of injected veins. Care should be taken to avoid high concentrations and prolonged contact with the drug, especially in patients who have elevated pressure in the antebrachial veins, such as those with mediastinal tumor compression. Extravasation of the drug into subcutaneous tissues results in painful inflammation with attending induration and sloughing. Infiltration of 0.16 molar solution of sodium thiosulfate together with application of an ice compress may minimize the local reaction.

The intravenous administration of mechlorethamine hydrochloride is accompanied by unpleasant side-reactions and possible damage to the hematopoietic system. Characteristic toxic effects are nausea, vomiting, and depression of the formed elements of the circulating blood.

Nausea and vomiting, which have sometimes been so severe as to precipitate vascular accidents in patients with a hemorrhagic tendency, usually occur 1 to 3 hours after administration of the drug. Emesis may disappear in the first 8 hours, but nausea can persist for 24 hours or longer. Anorexia, weakness, and diarrhea also may occur. Chlorpromazine hydrochloride, either alone or with a suitable barbiturate, is valuable in controlling the nausea and vomiting and should be administered 30 to 60 minutes prior to mechlorethamine injection and as long afterward as symptoms persist.

Lymphocytopenia followed by granulocytopenia occurs after the administration of mechlorethamine hydrochloride. Occasionally, agranulocytosis supervenes. Thrombocytopenia is variable, but it usually is present 2 to 3 weeks after completion of therapy. In some cases, this may lead to bleeding from the buccal mucosa and gastrointestinal tract, petechia, and subcutaneous hemorrhage. Erythrocyte and hemoglobin levels may decline during the first 2 weeks after therapy. This anemia is usually not significant; however, it should be borne in mind that depression of the hematopoietic system may last up to 50 days after institution of therapy. A subsequent course of nitrogen mustard therapy usually should not be undertaken for at least six weeks. The decision as to the time of institution of subsequent courses of therapy with nitrogen mustard depends upon the recovery of hematopoietic activity as evidenced by the appearance of the peripheral blood. Neither mechlorethamine therapy followed by x-ray nor x-ray therapy subsequent to the use of mechlorethamine should be employed until bone marrow function has recovered. This also applies when mechlor-

ethamine is similarly used with other cytotoxic compounds. Irradiation of such areas as the sternum, ribs, and vertebrae shortly after a course of nitrogen mustard may lead to severe hematological complications. Even if no other therapy has been employed previously, mechlorethamine should not be used in patients with severe leukopenia, thrombocytopenia, or anemia due to generalized direct invasion of bone marrow. A severe and even uncontrollable depression of the hematopoietic system may follow the administration of the usual therapeutic dose of mechlorethamine hydrochloride, particularly in patients with widespread disease and debility and in those patients who have had previous treatment with other similar agents or x-ray. If this occurs, therapy should be withdrawn and repeated transfusions, antibiotics, and general supportive measures should be administered.

Occasionally, a maculopapular skin eruption has been observed after mechlorethamine administration; this may be an idiosyncrasy and does not necessarily recur with subsequent courses. Herpes zoster has been reported, probably because a latent infection was present before therapy. In such cases, each course may be followed by overt manifestations of the viral disease.

Since the gonads are susceptible to mechlorethamine, a course of therapy may be followed by delayed menstruation or amenorrhea of several months' duration. No permanent damage to ovarian function has been observed, however. Impaired spermatogenesis has been reported in male patients at autopsy. In laboratory experiments, the nitrogen mustards have induced fetal abnormalities in pregnant mammals; thus these compounds should not be used if pregnancy exists or is suspected. They are likewise contraindicated in patients with coexistent or suspected infectious granuloma.

Dosage.—Mechlorethamine hydrochloride is administered only by the intravenous route. The drug is stable when kept in dry form, but solutions are unstable and decompose with standing. A fresh solution should therefore be prepared immediately before each injection. With a sterile 10-cc. syringe, 10 cc. of a suitable solvent, such as water for injection, is injected, with aseptic precautions, into a rubber-stoppered vial containing 10 mg. of dry powdered mechlorethamine hydrochloride. With the needle still in the rubber stopper, the vial is shaken to dissolve the drug. The resultant solution contains 1 mg. per cubic centimeter. The calculated volume of solution required for a single injection is then drawn into the syringe and injected into the rubber tubing of a flowing intravenous infusion, commonly of 250 cc. of isotonic sodium chloride solution or a 5% dextrose solution. The solution remaining in the vial should be discarded.

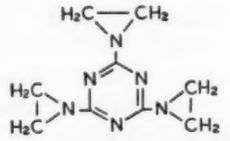
Dosage calculations of mechlorethamine hydrochloride are based upon body weight. It is important to take into consideration the presence of edema or ascites and to base the dosage on actual weight not complicated by these factors. A total dose of 0.4 mg. per kilogram of body weight for each course of therapy is usual in most cases. This is best given in divided doses of 0.1 mg. per kilogram on each of 4 successive days. The drug also has been given as two injections of 0.2 mg. per kilogram each on consecutive days without greater toxic reaction and with equal therapeutic response. Regardless of body weight, a single dose should not exceed 8 to 10 mg.

It should be emphasized that, since the margin of safety of mechlorethamine hydrochloride is extremely narrow, considerable care must be exercised in the matter of dosage. The usual average dose should be exceeded only with extreme caution; repeated blood tests are always mandatory as a guide to subsequent therapy.

Preparations for use as stated for the foregoing drug are marketed under the following name: Mustargen Hydrochloride.

Sharp & Dohme, Division of Merck & Co., Inc. cooperated by furnishing scientific data to aid in the evaluation of mechlorethamine hydrochloride.

Triethylene Melamine. — 2,4,6-tris(aziridine)-s-triazine. — 2,4,6-tris(ethylenimino)-s-triazine. — The structural formula of triethylene melamine may be represented as follows:



Actions and Uses.—Triethylene melamine is an ethylenimine derivative with actions and uses similar to those of the nitrogen mustards. (See the monograph on mechlorethamine hydrochloride.) It is converted in the body to a highly reactive quaternary ethylenimonium compound. Unlike the mustards, however, the conversion of triethylene melamine takes place in an acid rather than an alkaline medium; thus the drug may be administered orally. The cytotoxic actions of triethylene melamine are identical to those of the nitrogen mustards, and both drugs are believed to act in the same fundamental manner. Triethylene melamine, however, does not possess the local vesicant action of the nitrogen mustards, its onset and duration of action are more prolonged, and it produces less anorexia, nausea, and vomiting.

In general, the therapeutic indications for triethylene melamine are similar to those for nitrogen mustard therapy. As such, the drug is usually most effective for the palliative treatment of certain generalized, but not terminal, cancers of the lymphatic and hematopoietic systems. X-ray therapy is ordinarily considered the initial treatment of choice for localized tumor involvement. As patients generally become refractory to the drug, its effectiveness usually diminishes with continued use.

The best results to date with triethylene melamine have been obtained in patients with widely disseminated Hodgkin's disease. The drug should be employed as an adjunct to and not a substitute for irradiation therapy. It is particularly useful when localized lesions are not evident or when lesions recur quickly and spread in spite of x-ray therapy. Remissions induced by triethylene melamine are characterized by regression of tumor masses and relief from anorexia, weakness, and pruritus. Although these are of varied duration, temporary improvement lasting about 2 to 14 weeks can be expected in a significant percentage of patients. Subsequent triethylene melamine therapy usually is less effective.

Triethylene melamine is effective in some patients with generalized malignant lymphoma (lymphosarcoma) and chronic lymphocytic (lymphatic, lymphoid) leukemia. The response to the drug in these patients is usually not as satisfactory as in patients with Hodgkin's disease. In addition, the bone marrow of such patients appears to

be unusually susceptible to the drug, and severe depression of the hematopoietic system can result from small doses. Triethylene melamine therefore should be reserved for patients with conditions refractory to x-ray treatment or with neoplastic involvement too generalized to be amenable to conventional radiation therapy.

Although x-ray therapy, sodium radio-phosphate (P^{32}), and busulfan are considered more satisfactory for the treatment of chronic granulocytic (myelogenous, myeloid) leukemia, triethylene melamine may produce temporary remissions in certain cases. The drug should not be employed for the initial therapy of this disease but may be used when the response to the other therapeutic measures is poor. There is no evidence that triethylene melamine is effective in the treatment of acute leukemia.

There are isolated reports on the beneficial effects of triethylene melamine in mycosis fungoides, polycythemia vera, and carcinoma of the lung and ovary; however, sufficient experience with this agent has not been attained to justify its routine use in these conditions.

The clinical toxicity of triethylene melamine is identical to that of the nitrogen mustards, with the exception of a lower incidence of nausea and vomiting and the absence of local vesicant effects. The chief advantages of triethylene melamine are its oral effectiveness with less unpleasant side-effects and the feasibility of therapy on an ambulatory basis. The principal disadvantages are related to its slow onset of action and prolonged effect. Thus, though the drug initially is better tolerated than the nitrogen mustards, its cumulative toxicity is greater. In patients with severe constitutional symptoms, nitrogen mustard therapy would therefore appear to be preferable. Whenever triethylene melamine therapy is undertaken, the same precautions must be observed regarding depression of hematopoietic function as those described for mechlorethamine hydrochloride. It should be emphasized that any patient may be extremely sensitive to the effects of triethylene melamine and that extreme caution is indicated when bone marrow has been previously involved by disease or its function depressed by therapy.

Dosage.—Triethylene melamine is given orally in doses that must be determined individually. The extent to which it is absorbed appears to vary considerably. Since it is inactivated by excess gastric acidity and contact with food, it should be given with at least 2 gm. of sodium bicarbonate an hour or more before breakfast.

In initiating therapy, the usual maximum safe dosage is 2.5 mg. given on each of two successive mornings. Some patients, especially those with lymphosarcoma and chronic lymphocytic leukemia, are extremely sensitive to the effects of the drug. In such patients, anorexia may develop 8 to 12 hours after the second dose. If the second dose does not produce anorexia, it is usually safe to administer a third dose of 2.5 mg. The effects of the initial three doses on appetite and white blood cell count must then be observed for 3 to 5 days before more of the drug is administered. After this initial regimen, subsequent maintenance therapy with triethylene melamine is governed by the patient's sensitivity as evidenced by appetite and white blood cell count. Maintenance requirements vary from as little as 0.5 to 1 mg. every 7 to 14 days for patients with maximum sensitivity to as much as 2.5 to 5 mg. every 2 to 5 days in patients with low sensitivity. Total white blood cell counts should be recorded at least three times a week during the initial period and before every dose. Therapy should be suspended whenever the white blood cell count falls rapidly or is below 4,000. Any dose that causes severe anorexia or vomiting should be considered excessive. Because of slow onset of action, the therapeutic effect may not become evident until 7 to 10 days after initiation of therapy. Maintenance therapy should be continued, with leukocyte counts before each dose, as long as subjective improvement continues without evidence of excessive bone marrow depression. The initiation of therapy on a careful basis and its maintenance for a much longer period is essential for the successful employment of triethylene melamine.

Preparations for use as stated for the foregoing drug are marketed under the following name: Triethylene Melamine.

Lederle Laboratories Division, American Cyanamid Company, furnished scientific data to aid in the evaluation of triethylene melamine.

COUNCIL ON FOODS AND NUTRITION

The following announcement has been authorized by the Council on Foods and Nutrition.

EUGENE H. STEVENSON, M.S.
Acting Secretary.

SYMPOSIUM ON PROTEINS AND AMINO ACIDS

A symposium, "The Relation of Proteins and Amino Acids to Nutritional Health," jointly sponsored by the Los Angeles County Medical Association; University of California at Los Angeles School of Medicine; and the Council on Foods and Nutrition, will be held at Los Angeles, 9:30 a. m., Monday, May 21, 1956. The following program has been arranged, and the meeting will be open to all interested persons.

1. *Nitrogen Balance and the Nutritive Value of Proteins*
   James B. Allison, Ph.D., Rutgers University, New Brunswick, N. J.
2. *The Role of Vitamins in the Metabolism of Amino Acids*
   Otto A. Bessey, Ph.D., University of Texas School of Medicine, Galveston, Texas
3. *The Role of the Digestive Tract in the Utilization of Proteins and Amino Acids*
   E. S. Nasset, Ph.D., University of Rochester School of Medicine, Rochester, N. Y.
4. *The Amino Acid and Protein Requirements of Infants*
   E. L. Pratt, M.D., University of Texas, Southwestern Medical School, Dallas, Texas
5. *The Role of Hormones in Protein Metabolism*
   Robert E. Olson, M.D., University of Pittsburgh, Pittsburgh
6. *Malnutrition Due to Protein-Deficient Diets*
   Nevin S. Scrimshaw, M.D., Institute of Nutrition in Central America and Panama, Guatemala, Central America

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ENDOCRINE CONTROL OF PIGMENTATION

Skin pigmentation is a subject of broad interest. Racial difference in pigmentation, the protective action of sun-tan, and the sinister malignant melanoma are examples of the comprehensive nature of the problem. The dark pigment melanin, elaborated by the epidermal chromatophores, is an important determinant of skin color. In recent years, extensive clinical and laboratory investigations have greatly advanced our understanding of the biochemistry of melanin formation and have thrown considerable light on the mechanism by which changes in pigmentation may be produced.[1]

Melanin is an insoluble polymer of high molecular weight. The precursor of this pigment in vertebrates is tyrosine. Under the influence of the copper-containing enzyme tyrosinase, tyrosine is oxidized to dihydroxyphenylalanine, which is oxidized to the quinone of dihydroxyphenylalanine, with tyrosinase again serving as the enzyme. Subsequent oxidative steps lead to the formation of melanin.[2] In the normal unpigmented skin, the tyrosine-tyrosinase system exists in an inhibited state. In Negro skin and in malignant melanomas and in certain other physiological and pathological conditions, the inhibitory factor is removed and the reaction proceeds to completion.[3]

Certain of the factors influencing the tyrosine-tyrosinase reaction have been determined, while others are as yet only matters of speculation. Thus, albinism arises from a genetically transmitted lack of tyrosinase, while tyrosine deficiency is thought to cause the light skin and inability to sun-tan seen in individuals with phenylpyruvic oligophrenia, a genetically transmitted metabolic disorder in which the normal transformation of phenylalanine to tyrosine does not occur. Again, since the enzyme tyrosinase requires copper, factors that lead to a binding or deprivation of copper, such as the presence of sulfhydryl groups, may inhibit pigmentation, while conditions that favor the liberation of copper are conducive to increased pigmentation. Radiant energy is thought to lead to pigmentation through a reduction of sulfhydryl groups in the skin, while the heavy metals such as arsenic or bismuth may compete with copper on the sulfhydryl groups, or, if present in excess, may displace copper from the enzyme and thus may either increase or decrease pigmentation.

It has long been felt that certain endocrines play an important role in regulating skin color, as evidenced, for example, by the deep pigmentation seen in adrenal cortical hypofunction (Addison's disease) and the increased pigmentation that occurs during pregnancy. Furthermore, pigmentation may follow the administration of estrogens or of corticotropin but not of cortisone, while the pigmentation of adrenal cortical hypofunction frequently decreases appreciably with cortisone administration.

The role of the pituitary in pigmentary changes in certain fish, amphibians, and reptiles is well established. In such animals, removal of the pituitary leads to a permanent lightening, while injection of minute amounts of pituitary extract causes a rapid, transient darkening of the animal. The increased pigmentation is due to dispersion of the melanin within the melanophore under the influence of intermedin, a hormone elaborated in the intermediate lobe of most animals, or in the anterior lobe of those species that lack a discrete intermediate lobe.[4] It is also possible that intermedin accelerates the synthesis of melanin, or, alternately, that the dispersion of pigment induced by the hormone in some way facilitates the oxidation of melanin precursors, since frogs receiving large doses of intermedin for prolonged periods of time have an appreciably higher skin melanin content than controls who have received injections of saline solution.[5]

An immediate response to intermedin comparable to that observed in lower vertebrates has never been demonstrated in higher vertebrates, including man. Nevertheless the feeling has persisted that this hormone plays a role in human pigmentation. Recently Lerner and his associates [6] have reported darkening in human skin and nevi and the appearance of new nevi following prolonged administration of high doses of a partially purified preparation of intermedin.[6] Traces of corticotropin, oxytocin, and vasopressin were reported in this prepara-

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3. Lerner, A. B., and Fitzpatrick, T. B.: The Control of Melanogenesis in Human Pigment Cells, in Gordon, M.: Pigment Cell Growth: Proceedings of the Third Conference on Biology of Normal and Atypical Pigment Cell Growth, New York, Academic Press, Inc., 1953. Fitzpatrick, T. B., and Lerner, A. B.: Pigment and Pigment Tumors: Biochemical Basis of Human Melanin Pigmentation, A. M. A. Arch. Dermat. & Syph. **69**: 133 (Feb.) 1954.

4. Waring, H., and Landgrebe, F. W.: Hormones of the Posterior Pituitary, in Pincus, G., and Thimann, K. V.: The Hormones: Physiology, Chemistry and Applications, New York, Academic Press, Inc., 1950, vol. 2.

5. Frieden, E. H., and Bozer, J. M.: Effect of Administration of Intermedin upon Melanin Content of the Skin of Rana pipiens, Proc. Soc. Exper. Biol. & Med. **77**: 35, 1951.

6. Lerner, A. B.; Shizume, K., and Bunding, I.: The Mechanism of Endocrine Control of Melanin Pigmentation, J. Clin. Endocrinol. **14**: 1463, 1954. Shizume, K., and Lerner, A. B.: Determination of Melanocyte-Stimulating Hormone in Urine and Blood, ibid. **14**: 1491, 1954.

7. Edwards, E. A.: Analysis of Skin Color in Living Human Subjects by Spectrophotometric Means, in Pigment Cell Growth: Proceedings of the Third Conference on Biology of Normal and Atypical Pigment Cell Growth, Gordon, M., editor, New York, Academic Press, Inc., 1953.

tion, but the presence or absence of other possible contaminants was not indicated. These investigators suggest the increased pigmentation often seen in corticotropin therapy is due to the presence of contaminating melanophore hormone and that the hyperpigmentation seen in adrenal cortical hypofunction is due to increased pituitary secretion consequent to the release of adrenal inhibition. Conversely they consider that the decreased pigmentation often associated with panhypopituitarism is due to the loss of melanophore hormone. In substantiation of this theory, they found elevated titers of melanophore hormone in the blood and urine of pregnant patients, of patients in whom bilateral adrenalectomy had been done, and of patients with adrenal cortical hypofunction. Normal values were found in normal Negroes, in albinos, and in patients with vitiligo, while decreased amounts were found in two of eight patients with decreased pituitary function. Furthermore, they found cortisone administration to a patient with high blood and urinary intermedin levels reduced the increased titers to normal. However, since their bioassay procedure permits the recovery of only 20% of an added amount of hormone, the increased values do not necessarily reflect an increased elaboration of the hormone.

In addition, it must be borne in mind that other pigments; namely, carotene, oxyhemoglobin, reduced hemoglobin, and melanoid, a melanin-like pigment, also contribute to skin coloration. Spectrophotometric measurements have been developed that permit the identification and approximation of these various pigments under varying conditions. Such studies indicate, for example, that changes in cutaneous blood flow may play an important role in pigmentary changes associated with hormonal deficiencies or administration of certain endocrine preparations.[7] Thus, while a role by the melanophore hormone in human pigment is an intriguing possibility, it cannot be considered as established at this time.

AGREEMENT BETWEEN UMWA WELFARE AND RETIREMENT FUND AND MEDICAL SOCIETY OF STATE OF PENNSYLVANIA

THE JOURNAL is pleased to reproduce (this issue, page 164) the agreement entered into between the United Mine Workers of America Welfare and Retirement Fund and the Medical Society of the State of Pennsylvania. All physicians can be encouraged by the fact that one medical society through diligent effort has faced up to a problem and through round-table discussion entered into a written agreement that seeks to accomplish resolution of a thorny problem facing its members.

This does not mean that all problems have been solved, as Dr. Meiser, chairman of the society's committee on medical economics, stated in a recent talk before the Pennsylvania Secretaries and Editors Conference: "It would be a blundering fallacy indeed, if we, who were instrumental in compiling this agreement, believed that it immediately solved all the problems before us. We do believe it does, in a good measure, prevent some unwise restrictions and regulations which would threaten not only our professional freedom, but deter us from giving that high quality of medical care which the people of Pennsylvania so justly deserve. We wish to assure you here and now, that any constructive criticism, or any suggestions that may improve what has been done, will be gratefully accepted and given very serious consideration. This is your agreement, for you are the Medical Society of the State of Pennsylvania."

It is, however, the culmination of months of consultation and conference, and the efforts of the medical society and the results of those efforts can be commended to the attention and study of all who wish to improve relations between medicine and employer or employee groups.

GOOD NEWS FROM BRITAIN

Self-employed professional persons in Great Britain and in the United States have been discriminated against for many years in pension tax matters. Lacking an employer-employee relationship, they have not been able to establish individual retirement systems under which the amount set aside for old age each year does not become taxable until withdrawn during retirement. At long last the situation, at least in Britain, is about to be relieved. The Chancellor of the Exchequer in his budget speech before Parliament on April 17 recommended—which is tantamount to adoption—superannuation tax relief in the following words:

"I now pass to another aspect of saving. I propose to give effect, though in a simplified and modified way, to the recommendations of the Second Millard Tucker Committee on relief to the self-employed in respect of provision for retirement.

"This will grant relief from income tax and surtax, within certain limits, in respect of premiums paid to provide a deferred annuity on retirement. The relief will apply to professional men in practice, to individuals and partners who are not companies, to controlling directors of companies and finally to employees who are not entitled to any benefit under schemes set up by their employers. It will be a condition of relief that the benefits secured by the premiums shall be payable only as annuities and not as lump sums.

"The relief will be limited to premiums not exceeding £500 or 10 per cent. of earned income in any one year."

When these recommendations are enacted into law, the British physician will no longer need to be an employee in order to enjoy favorable conditions for saving for his retired years. Henceforth, as a self-employed physician he can defer income taxes until retirement on the amounts, up to a modest annual limit of £500, he has set aside during his working years. In an era of fringe benefits for employed persons, this good news from Britain will encourage self-employed physicians in the United States to hope that the income tax discrimination against them will be removed in due time.

ORGANIZATION SECTION

REPORTS OF OFFICERS

The following reports will be presented to the House of Delegates of the American Medical Association at its session to be held in Chicago in June.

REPORT OF THE BOARD OF TRUSTEES

To the Members of the House of Delegates of the American Medical Association:

The following report of the Board of Trustees is respectfully submitted:

Financial Statement

The official 1955 reports of the Treasurer and the Association's auditors appear as a part of this report of the Board of Trustees.

American Medical Association dues collections through the constituent state and territorial associations amounted to $3,257,685 and again represented more than 99% of the potential dues of the Association.

Subscription receipts from THE JOURNAL and the specialty journals, which includes an allocation of dues from members and receipts from subscriptions to *Today's Health,* amounted to $3,558,484, exceeding 1954 receipts by approximately $61,000.

Advertising revenue exceeded 1954 by $426,000 and amounted to $4,184,277. THE JOURNAL and specialty journals gained $418,000 and *Today's Health* $8,000. Investments of the Association earned $239,298 in 1955 compared with $212,461 in 1954. The approximate over-all yield was 3%. Miscellaneous receipts amounted to $24,790.

Printing and publishing costs of Association periodicals and pamphlets amounted to $4,959,660, an increase over 1954 of $277,621, represented by increased production, higher plant wages and paper costs.

Expenditures of Councils, Bureaus, and related activities listed in Schedule 1 of the Auditor's report amounted to $3,642,120, an increase of $138,000 over 1954.

The cost of conducting the Annual Meeting at Atlantic City and the Clinical Meeting at Boston after credit for sale of Technical Exhibit space amounted to $42,513. The 1954 meetings held in San Francisco and Miami cost $105,721.

Cash discounts allowed in excess of discounts received amounted to $60,666 compared with $56,145 for 1954. This increase of $4,521 represents discounts allowed on increased advertising sales.

Depreciation and taxes unallocated of $27,868 approximates the 1954 figure and represents depreciation and local taxes only on headquarters office equipment. Building and machinery depreciation and real estate taxes are direct operational expenses and are not included in this amount. Legal expenses amounted to $44,610 compared with $85,131 for the previous year.

The Association again appropriated $100,000 from 1955 income as a contribution to the American Medical Education Foundation. Total Association contributions to the Foundation amount to $2,200,000.

An increase in gross income for 1955 over 1954 is indicated as $532,356. Operating and other costs increased $313,765. Income in excess of expense for 1955 amounted to $454,023 compared with $235,432 for 1954.

Association properties and equipment, not including land, after allowance for depreciation, show a net book value of $1,666,284. The reserve for depreciation has been increased to $1,789,578 from $1,706,310.

Marketable securities carried at cost are valued at $6,516,593 exclusive of securities held in the American Medical Association Research Fund of $1,494,100, the total amounting to $8,010,693 at Dec. 31, 1955, and compares with $7,379,130 at Dec. 31, 1954. A general classification of securities will be found in the balance sheet contained in the Auditor's report. Marketable securities on Dec. 31, 1955, in the amount of $6,516,593 represent investments of:

American Medical Education Foundation Fund	$ 100,000
General Fund	2,426,593
Depreciation Reserve Fund	1,790,000
Association Reserve Fund	350,000
Retirement Reserve Fund	150,000
Building Reserve Fund	1,000,000
Equipment Modernization Reserve Fund	700,000

Report on Matters Referred by House of Delegates

Military Status for Public Health Service.—In June, 1955, the House of Delegates referred to the Board of Trustees Resolution No. 1, which recommended that legislation be enacted by the Congress designating the Public Health Service as a component branch of the armed forces on an equal status with the Army, Navy, and Air Force. On recommendation of the Committee on Legislation, the Board of Trustees voted to approve S. 2587, 84th Congress. This bill carries out the provisions of the resolution.

Chamber of Councillors.—As requested by the House of Delegates at its meeting in Boston, the Board of Trustees reviewed the resolution recommending the establishment of a chamber of councillors to American medicine. A plan similar to that suggested in the resolution was considered by the Board some years ago. On looking into the matter at that time, it was found that implementation of such a proposal was not feasible but that, instead, it would be wise to call on qualified persons outside of the medical profession for counsel on an "ad hoc" basis whenever such advice was necessary. The Board is still of the same opinion and recommends, therefore, that the resolution be not adopted.

Voice of America and Radio Free Europe.—In response to the resolution requesting the Board of Trustees to cooperate fully with the Voice of America and Radio Free Europe programs, the Board wishes to report that for the past eight years the Association has cooperated with the Voice of America. In 1951, the Bureau of Health Education recorded thirty 15-minute tapes for broadcast by that program, and this series was incorporated in its University of the Air program. Twenty-four of these programs were selected for broadcast to Europe, the Far East, and South Asia. At the Annual Meeting in New York City in 1953, the Association produced eight recordings for the Voice of America by foreign doctors who attended the meeting. These programs were three or four minutes in length and consisted of personal greetings from the foreign physicians to be sent back to their homelands. In accordance with the action of the House of Delegates in Boston regarding the Voice of America and Radio Free Europe programs, the Department of Public Relations plans to develop a closer liaison with these two groups.

Improvement of the Care of the Patient.—Supplementary report I of the Board of Trustees to the House of Delegates at its meeting in Boston recommended that "the physicians of the United States . . . do everything possible to improve patient care, cooperate with all groups involved in improvement of patient care, and accept the responsibility for providing the necessary leadership for establishing Joint Committees for the Improvement of the Care of the Patient at state and local levels." The report of the reference committee, which was adopted by the House, requested definition and clarification of what groups would constitute the joint committees and recommended consultation with representatives of the College of American Pathologists.

Following the directive of the House, the Board contacted the College of American Pathologists, advising it of the composition of the national Joint Commission for the Improvement of the Care of the Patient and its method of operation, stating that the intent of the resolution was to encourage the establishment of state and local commissions and requesting its comments. The

Board recommends the addition of the following sentence to its previous report, which it is believed will carry out the request of the House for clarification: "The state and local committees, patterned after the national group, would be composed of representatives from the medical profession, hospital administrators, and nurses."

Council on Medical Physics

At its meeting in Boston Nov. 29 to Dec. 2, 1955, the House of Delegates adopted a report of the Board of Trustees that recommended that a Council on Medical Physics be established to "carry on activities in the field of apparatus, instruments, and devices." The new Council replaces the former Council on Physical Medicine and Rehabilitation.

The Council on Medical Physics will be composed of 13 members selected from various fields of medicine. They have been chosen because of the special knowledge that they have and not as representatives of specialties. The members appointed are:

FRANK H. KRUSEN, Chairman, Rochester, Minn.
WARDE B. ALLAN, Baltimore.
ALFRED BLALOCK, Baltimore.
FREDERICK C. BOST, San Francisco.
RICHARD CHAMBERLAIN, Philadelphia.
ANTHONY C. CIPOLLARO, New York.
OTTO GLASSER, Cleveland.
MARION R. MOBLEY, Florence, S. C.
HANS H. REESE, Madison, Wis.
GEORGE J. THOMAS, Pittsburgh.
DERRICK VAIL, Chicago.
GEORGE E. WAKERLIN, Chicago.
SHIELDS WARREN, Boston.

Committee on Rehabilitation

In considering the report of the Board of Trustees relative to the establishment of a Committee on Rehabilitation, the House of Delegates in Boston amended the report to read:

It is believed that rehabilitation problems should be assigned to an *intra*-association liaison group with representation from all interested American Medical Association councils, *sections* and committees dealing with the subject. (changes italicized)

The functions and interests of the councils of the House of Delegates and of the Board were reviewed, and it was agreed that one representative from the Council on Medical Service, Council on Medical Education and Hospitals, Council on Mental Health, Council on Industrial Health, Council on Medical Physics, Council on Foods and Nutrition, and the Bureau of Health Education should constitute the Committee on Rehabilitation.

The Board recommends that the House of Delegates give consideration to rescinding its action including representation from the scientific sections for two reasons: (1) the scientific sections are not autonomous organizations within the structure of the Association, and (2) if representation is to be included from all interested sections, the Committee on Rehabilitation would become unwieldy and, consequently, ineffective.

Scientific Sections

With a view to determining the proper activities and functions of the scientific sections, the Board of Trustees requested a review of the pertinent sections of the Constitution and Bylaws of the Association.

This review indicates that Article IX of the Constitution of the American Medical Association provides for the organization of a Scientific Assembly of the Association. The Scientific Assembly is defined as the meeting of the members for the purpose of discussing subjects pertaining to the science and art of medicine. It is divided into a number of sections, each section representing a specialized segment of the practice of medicine. If present sections are to be discontinued or new sections added, the Board of Trustees is directed to study the problem and make a recommendation to the House of Delegates, which then makes the final determination in the matter. Meetings of the Scientific Assembly, and of its several sections, are to be held annually and are to be conducted in accordance with rules and regulations set forth in the Bylaws.

Division Two of the Bylaws, Chapters V through VIII, sets forth in some detail the methods designed for the practical functioning of the Scientific Assembly and its several sections. Persons entitled to register are classified, and provision is made for the holding of General and Inaugural meetings. Then the specific sections are named, and the officers which they may elect are designated. These officers have the primary responsibility of arranging a program for section meetings and assisting the Board of Trustees in obtaining outstanding exhibits pertaining to their particular specialty. The executive committee of a section approves or disapproves for publication the papers read before the section. Also covered in the Bylaws are such questions as who may read papers, who may participate in section work, what standards shall be considered when recommending a paper for publication, who has the property right in papers presented to sections, etc.

The entire concept of the Scientific Assembly is founded on the need of a forum for the discussion and dissemination of scientific information. Anything other than scientific matters would seem to have no place in its deliberations. The thought that the Scientific Assembly and its several sections should concern themselves only with scientific matters is strengthened by the further fact that the business and legislative interests of the Association are regulated in a totally different division of the Bylaws, Division Three.

In summary, it seems clear from the provisions of both the Constitution and the Bylaws that the purpose of the Scientific Assembly is to provide a forum for a discussion of the scientific aspects of medical practice. All other aspects, social, political, economic, etc., are within the purview of the House of Delegates.

Membership of Council on Medical Service

At its meeting in March, the Council on Medical Service recommended to the Board of Trustees that consideration be given to (1) changing the elected membership of the Council from six to nine, and (2) the advisability and feasibility of continuing the present role of ex officio members and the present requirement that the immediate Past President serve on the Council. The Council feels that its work would be facilitated and would be less of a hardship on its members if there were nine elected members rather than six as at the present time.

The Board of Trustees concurs in the recommendation of the Council on Medical Service and transmits it to the House of Delegates for consideration and appropriate action. For the convenience of the delegates, the portion of the Bylaws pertaining to membership on the Council on Medical Service is quoted below:

The Council on Medical Service shall include six Active or Service Members. All members shall be elected by the House of Delegates for terms of five years so arranged that at one annual session the terms of two members expire and at four annual sessions the term of one member expires. In addition, the President, the immediate Past President, and a member of the Board of Trustees selected by the Board shall be members of the Council, except that the President and the Trustee member shall be ex officio members without vote.

Accreditation of Hospitals

Dr. Raymond F. Peterson, Butte, Mont., a member of the House of Delegates, has been selected to fill the unexpired term of Dr. Rolland Whitacre as one of the representatives of the American Medical Association on the Joint Commission on Accreditation of Hospitals.

Annual and Clinical Meetings

The following places and dates have been approved by the House of Delegates and the Board of Trustees for the Annual and Clinical Meetings of the Association:

Annual Meetings: 1957—New York, June 3-7; 1958—San Francisco, June 23-27; 1959—Atlantic City, June 8-12; 1960—Chicago, June 6-10.

Clinical Meetings: 1956—Seattle, Nov. 27-30; 1957—Philadelphia, Dec. 3-6; 1958—Minneapolis, Dec. 2-5.

Supplementary Reports

Supplementary reports on certain subjects that have been referred to the Board of Trustees by the House of Delegates and on other matters of interest to the House will be presented at the first meeting in Chicago.

Respectfully submitted,

GUNNAR GUNDERSEN, Chairman.
F. J. L. BLASINGAME, Vice-Chairman.
EDWIN S. HAMILTON, Secretary.
JULIAN P. PRICE.
JAMES R. REULING.
JAMES R. McVAY.
DAVID B. ALLMAN.
LEONARD W. LARSON.
THOMAS P. MURDOCK.
ELMER HESS.
DWIGHT H. MURRAY.

AUDITOR'S REPORT

March 6, 1956

The Board of Trustees, American Medical Association:

We have examined the balance sheet of the American Medical Association as of Dec. 31, 1955, and the related statement of income for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances.

In our opinion, the accompanying balance sheet and statement of income present fairly the financial position of the American Medical Association at Dec. 31, 1955, and the results of its operations for the year then ended, in conformity with generally accepted accounting principles which, except for the changes (of which we approve) in the methods of recording certain subscription receipts and commissions thereon as explained in the note to financial statements, have been applied on a basis consistent with that of the preceding year.

PEAT, MARWICK, MITCHELL & Co.

BALANCE SHEET—DEC. 31, 1955

Assets

Cash			$ 474,757
Accounts receivable:			
Advertising	$ 331,824		
Directory report service—19th edition	26,217		
Other	70,865		428,906
Interest accrued on investments			41,051
Inventories of materials, supplies, work in progress, and publications, at cost			408,870
Expenditures on publications in progress			190,362
Prepaid expenses, deposits, and advances:			
Deposits and advances	78,841		
Commissions applicable to unexpired subscriptions to publications (see note)	351,988		
Insurance and other prepaid expenses	26,107		456,936
Marketable securities, at cost (value based on market quotations of $6,915,674):			
United States Government securities	3,688,815		
Public utility and industrial bonds	1,502,658		
Common stocks	1,325,120		6,516,593
Representing investments of:			
American Medical Education Foundation Fund	$ 100,000		
General fund	2,426,593		
Depreciation reserve fund	1,790,000		
Association reserve fund	350,000		
Retirement reserve fund	150,000		
Building reserve fund	1,000,000		
Equipment modernization reserve fund	700,000		
American Medical Association Research Fund:			
United States Government securities, at cost (value based on market quotations of $1,441,728)		1,493,779	
Cash		321	1,494,100
Property, plant, and equipment, at cost:			
Land		453,774	
Building	2,186,459		
Machinery and printing equipment	714,156		
Office and laboratory equipment	555,248		
	3,455,863		
Less allowance for depreciation	1,789,578	1,666,285	2,120,059
			$12,131,634

See accompanying note to financial statements.

Liabilities

Accounts payable and accrued expenses:			
State Journal Advertising Bureau			$ 52,465
Other accounts payable			350,995
Accrued payroll			59,240
Accrued taxes			91,996
Employees' withheld taxes			51,818
			606,514
Provision for payment to American Medical Education Foundation			100,000
Provision for completion costs of cumulative index volumes to be issued, less amount recoverable by subscription of $136,692			213,649
Deferred credits:			
Unexpired subscriptions to publications (see note)	$1,354,048		
Income from 19th edition directory report service, less accumulated costs applicable to directory	159,719		
Other, including 1956 dues of $20,600 received in advance	34,442		1,548,209
American Medical Association Research Fund reserve			1,494,100
Other reserves:			
Association	350,000		
Retirement	150,000		
Building	1,000,000		
Equipment modernization	700,000		2,200,000
Capital account:			
Balance at December 31, 1954	5,507,634		
Add (deduct):			
Cash collections on subscriptions to periodical publications applicable to prior years	$387,774		
Adjustment of recoverable costs of cumulative index volumes applicable to prior years	40,929		
Unexpired portion of certain subscriptions at January 1, 1955, less certain prepaid commissions at that date (see note)	(421,198)	7,505	
Income in excess of expenses for the year ended December 31, 1955		454,023	5,969,162
			$12,131,634

STATEMENT OF INCOME

YEAR ENDED DEC. 31, 1955

Income:		
Membership dues and subscriptions to periodical publications (see note)		$4,924,307
Advertising		4,184,277
Income from investments		239,298
Miscellaneous receipts and other income, net		24,790
		9,372,672
Expenses:		
Printing and publication costs of periodicals, books, and pamphlets	$1,959,660	
Councils, bureaus, and related activities (Schedule 1)	3,642,120	
Employees' past service retirements	41,209	
Annual and interim meetings, net	42,515	
Cash discounts, net	60,666	
Depreciation and taxes—unallocated	27,869	
Legal	44,610	
	8,818,649	
Appropriated for American Medical Education Foundation	100,000	8,918,649
Income in excess of expenses		$ 454,023

See accompanying note to financial statements.

NOTE TO FINANCIAL STATEMENTS

Commencing with the year 1955 the Association adopted the accrual basis of accounting for (1) the unexpired portion of subscription receipts on THE JOURNAL of the American Medical Association and on the specialty journals and (2) the paid commissions applicable to unexpired subscriptions to *Today's Health*. Accordingly, the capital account was charged with an amount of $421,198, representing the unexpired portion of these subscription receipts at Jan. 1, 1955, $589,198, less the prepaid commissions at that date, $168,000. At Dec. 31, 1955, the unexpired portion of subscription receipts less the prepaid commissions amounted to $237,210.

COUNCILS, BUREAUS, AND RELATED ACTIVITIES

EXPENSE FOR YEAR ENDED DEC. 31, 1955

Secretary's office	$ 92,470
Association activities	338,893
Association trustees	11,885
Membership records	213,714
Law department	108,225
Biographical records	186,746
American Medical Education Foundation	110,264
Department of Public Relations	425,692
Washington Office of A. M. A.	207,227
Chemical laboratory	89,063
Microbiologic laboratory	5,026
Council on Medical Education and Hospitals	363,457
Council on Medical Service	180,281
Council on Pharmacy and Chemistry	152,413
Council on Medical Physics	70,204
Council on Foods and Nutrition	45,003
Council on Industrial Health	81,355

Council on National Defense	38,911
Council on Rural Health	62,074
Council on Constitution and Bylaws	2,622
Judicial Council	11,399
A. M. A. Library	74,551
Bureau of Exhibits	96,859
Bureau of Health Education	267,944
Bureau of Investigation	39,861
Bureau of Medical Economic Research	210,040
Committee on Cosmetics	20,485
Committee on Mental Health	44,921
Committee on Research	50,701
Committee on Legislation	25,374
Committee on Medicolegal Problems	8,510
	$3,642,120

TREASURER'S REPORT

INVESTMENT ACCOUNT

REPORT OF THE TREASURER OF THE AMERICAN MEDICAL ASSOCIATION FOR THE YEAR ENDED DEC. 31, 1955

Investments at beginning of year (at cost)		$5,885,030.43	
Bonds purchased	$7,144,464.38		
Common stocks purchased	603,843.29	7,748,307.67	
		$13,633,338.10	
Less:			
Bonds called, matured, or sold	$6,194,182.88		
Common stocks sold	922,562.24	$7,116,745.12	
Investments at end of year (at cost)			$6,516,592.98
Cash in bank at beginning of year		$ 8,087.54	
Interest and dividends received	$ 205,429.79		
Less interest prepaid on current year's bond purchases	9,882.94	195,546.85	
		203,634.39	
Transferred to general fund		165,000.00	
Cash in bank at end of year			38,634.39
Cash in bank and investments at end of year			$6,555,227.37

DAVIS MEMORIAL FUND

Funds on deposit at Jan. 1, 1955	$8,919.16	
Interest earned on bank balance in 1955	134.29	
		$9,053.45

RESEARCH FUND

Investments at beginning of year (at cost)		$1,493,778.76	
Bonds matured and purchased:			
U. S. Treasury Bonds matured Series G 2½% maturity 1/1/55	$100,000.00		
U. S. Treasury Bonds purchased Series K 2.76% due 1/1/67	100,000.00		
		$1,493,778.76	
Cash in bank at beginning and end of year		321.24	
Cash in bank and investments at end of year			$1,494,100.00
Interest received on investments and transferred to general fund to apply on research expenditures	$ 36,283.75		

JOSIAH J. MOORE, Treasurer

REPORT OF THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

To the Members of the House of Delegates of the American Medical Association:

As a result of action of the House of Delegates in June, 1954, the Council on Medical Education and Hospitals initiated the formation of the Cooperating Committee on Graduates of Foreign Medical Schools. This Committee was charged with devising an effective and equitable mechanism for evaluating the medical qualifications of foreign-trained physicians who wished to come to this country. The Cooperating Committee has formulated a program that has gained approval, in principle, of the Board of Trustees of the American Medical Association, the Board of Trustees of the American Hospital Association, the Federation of State Medical Examining Boards, and the Executive Council of the Association of American Medical Colleges.

The Council on Medical Education and Hospitals presents this report so that the House of Delegates may be informed of the program proposed for evaluating graduates of foreign medical schools and some of the activity that led to the development of this program.

Introduction

Recent political and social events here and abroad have led to a continuing inflow into the United States of large numbers of foreign-trained physicians. The majority of such physicians enter this country on temporary student visas seeking further education. The remainder come as immigrants on permanent visas or are American citizens who have studied medicine abroad.

Foreign-trained physicians who enter the United States for further training for the most part acquire that training as interns or residents. Almost all who enter as immigrants or as citizens returning from the study of medicine abroad also accept positions in American hospitals, since an approved internship in the United States is a prerequisite to most licensure examinations for graduates of foreign medical schools. Internships and residencies in hospitals in the United States are primarily designed as a further part of the education of graduates of American medical schools. This further education is deliberately structured to give the medical school graduate, prior to entering practice, additional experience in dealing with patients including the assumption of increasing responsibility for the care of those patients. There has long been general agreement that this experience cannot be of real educational value unless the element of responsibility for patient care is present.

Since the beginning of this century, the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical Colleges have carried on an accreditation program that has made possible the maintenance of intimate and continuous knowledge of the standards of medical education and level of expected academic achievement in medical schools in the United States and Canada. This medical school accreditation process renders reasonable assurance that graduates of American medical schools are capable of assuming the patient care responsibilities that characterize internship and residency positions. It is admittedly impossible to acquire and continuously maintain similar intimate knowledge of all components of the educational program in medicine in all of the countries that are potential sources of physician emigrees or physicians seeking further training in this country.

Thoughtful physicians are aware of and in sympathy with the traditions of the United States and do not desire to seek any change that would exclude alien physicians from this country. It is firmly believed, however, that the medical profession and associated groups interested in the health and welfare of the nation have the obligation to be in a position to give assurance that foreign-trained physicians who assume intern or residency responsibilities in American hospitals have qualifications and capabilities similar to those of graduates of approved schools in the United States and Canada.

Thus the problem has arisen of devising a means of evaluating graduates of foreign medical schools who seek positions as interns or residents in U. S. hospitals in order that reasonable assurance can be given in regard to their competence as compared to graduates of American and Canadian approved schools.

Cooperating Committee on Graduates of Foreign Medical Schools

At the June, 1954, meeting of the American Medical Association, after considering resolutions Nos. 27, 38, and 54 and a supplementary report of the Board of Trustees, all dealing with the problem of foreign-trained physicians, the Reference Committee on Medical Education and Hospitals recommended and the House of Delegates approved "that the intent and aims of the supplementary report and the three resolutions can best be met by referring the entire problem to the Council on Medical Education and Hospitals for further study." Shortly after this action by the House of Delegates, the Council on Medical Education and Hospitals initiated the formation of the Cooperating Committee on Graduates of Foreign Medical Schools. This Committee has since its onset consisted of representatives of the Council on Medical Education and Hospitals of the American

Medical Association, the American Hospital Association, the Association of American Medical Colleges, and the Federation of State Medical Examining Boards. As a result of continuous study and numerous meetings during its year and a half of existence, the Cooperating Committee has formulated a program which it believes offers a sound and equitable solution to the problems presented to it.

The following principles gave guidance and direction to the Cooperating Committee in its considerations. It is believed that these principles should similarly give guidance in the administration of the proposed program of the Committee.

1. Although the responsibility to share educational opportunities in medicine is recognized, the primary concern must be for the health care of the American public. Thus, before assuming responsibility for the care of patients as interns or residents, all graduates of foreign medical schools (immigrants, exchange students, and American graduates of foreign medical schools) should give evidence, as nearly as can be measured, of having reached a level of educational attainment comparable to that of students in American schools at the time of graduation.

2. The primary objective of this Committee is to devise an effective mechanism for measuring educational attainment in the absence of intimate and continuing knowledge of the educational background of foreign-trained physicians. This mechanism should provide hospitals with pertinent information regarding the medical qualifications of foreign-trained physicians seeking positions as interns or residents. It should not interfere with the hospital's privilege of making its own selection among qualified physicians, nor should it serve as a substitute for or interfere with the normal licensure procedures of the various state boards.

3. It is not intended that this mechanism be applicable to those foreign medical school graduates in this country as temporary students participating in programs of medical and related studies in recognized universities, medical schools, and postgraduate schools, who by the very nature of their study are not involved in the responsibility of patient care.

It is the belief of the Cooperating Committee that acceptance and implementation of its proposed program will afford hospitals needed assurance in regard to the medical qualifications of foreign-trained physicians seeking positions as interns and residents. This program represents an extension to foreign graduates of the same principle that has proven its value and long been in effect for American graduates.

The Proposed Program

The emphasis in this program is placed on evaluating the medical qualifications of the individual foreign-trained physician who wishes to come to the United States, rather than attempting to evaluate on a continuing basis the educational programs of the hundreds of foreign medical schools that serve as potential sources of these foreign-trained physicians.

The program is designed to establish two principal criteria in regard to each such foreign-trained physician: (1) that he is a graduate of a bona fide medical school; (2) that, as nearly as can be measured, he has reached a level of educational attainment comparable to that of students in American schools at the time of graduation.

These criteria are to be established by evaluation of the foreign-trained physician's medical credentials in view of predetermined minimal standards and examination of the foreign-trained physician for factual knowledge of medicine.

Evaluation of Medical Credentials

The basic requirements listed below must be met in order for the foreign-trained physician's credentials to be considered satisfactory. As evidence of fulfillment of these requirements, the candidate should present medical credentials in original form with an acceptable English translation. These credentials together with the bona fide status of the medical school should be verified by the American Consul in the country in which the school of graduation is located.

Basic Requirements

1. A minimum of 18 years of total formal education.

2. Included in this minimum of 18 years of total formal education should be a minimum of 32 months of attendance and direct study of medicine excluding any time devoted to what in the United States would be considered as premedical study or internship.

3. In any country where the minimum standards stated above do not constitute sufficient educational achievement to acquire licensure in that country, the latter rather than the minimum previously described would be required. Although it would be expected that licensure would be achieved in the country in which is located the school of graduation, under exceptional circumstances such licensure would not be demanded if the candidate had fulfilled all of the educational requirements for licensure.

4. Evidence of satisfactory completion of the above described courses of study.

5. As evidence of acceptable moral and ethical behavior, each candidate must present a properly executed affidavit that he has not been convicted of any crime involving moral turpitude, and that he has never been censored or had other punitive action taken against him for reasons of immoral conduct by any recognized medical body including licensing agencies.

Examination for Factual Knowledge in Medicine

The objectives that this program is designed to fulfill dictated certain factors that had to be considered in determining the nature of the examination.

1. An acceptable examination must be a valid test of the foreign physician's factual knowledge in medicine. The examination must also give sufficient insight into the applicant's ability to approach rationally a clinical problem and follow it through to a logical conclusion as the result of application of basic medical concepts rather than empiric knowledge.

2. Since applicants to this evaluation service are to be measured in comparison to the performance of graduates of American medical schools, the examination must lend itself to such a comparison.

3. If this program is widely accepted, as the Committee is confident it will be, foreign-trained physicians seeking further training in the United States will not be able to find positions offering such experience until they have successfully completed all phases of the program. Those physicians seeking further training in the United States cannot obtain a student visa until they have already received a position offering this additional training. It therefore is necessary that the examination be conducted abroad as well as in the United States. Under these circumstances it is then also most advisable that the administration of the examination require minimal supervision.

4. The costs of preparation and administration of the examination must not be prohibitive.

On the basis of advice from consultants experienced in educational testing, the Cooperating Committee concluded that an objective type examination of approximately 400 properly selected test items would provide for purposes of this program a valid measure of medical knowledge. A significant number of these items should consist of case presentations with multiple questions based on them to determine the applicant's ability to interpret symptoms, signs, and basic laboratory data in arriving at accurate diagnoses and rational therapy. Such an examination could be given in a single day, divided into a morning and an afternoon session.

Utilization of the objective multiple-choice examination presents many advantages. Perhaps most important among these for the purposes of this program is that such an examination lends itself to rapid, accurate, impartial machine scoring and thorough statistical analysis, thus providing a sound basis for many comparative studies. Another important advantage of this type of testing is that the administration of it is not complex and only minimal supervision is necessary so that it could be given abroad.

One of the important problems that has been encountered with graduates of foreign medical schools who have taken further training in hospitals in this country has been their lack of satisfactory command of English. Inability to communicate well with colleagues, staff physicians, and patients can readily lead to disastrous accidents in patient care. Furthermore, it is highly unlikely that any effective learning can occur without easy intercommunication between student and teacher. Facility with English is to be one of the requirements for participation in this program and will be one of the factors measured.

Successful completion of all phases of this evaluation program would result in certification of this achievement to hospitals and other interested organizations with the approval of the foreign-trained physician concerned.

ADMINISTRATIVE PLANNING

It is proposed that an organization entitled "Evaluation Service for Foreign Medical Graduates" be formed as a not-for-profit corporation to administer this program. The property, business, and affairs of this corporation should be managed by a Board of Trustees composed of representatives of the American Medical Association, American Hospital Association, Federation of State Medical Examining Boards, and Association of American Medical Colleges.

The Cooperating Committee has made rather detailed studies of the needs in the areas of administrative organization, staff, methods of administering the evaluation of credentials and the examination, and finances. The Committee has reached certain recommendations in all of these areas and plans to turn over to the organization to be created to conduct this program all of its studies and recommendations.

It is apparent that for this program to be initiated funds will have to be available. The Cooperating Committee is of the opinion that the need for an effective mechanism to evaluate graduates of foreign medical schools seeking positions in our hospitals is widely recognized. It is confident that the program it has planned is basically sound and that it will be possible to obtain the financial support required to initiate it. The Committee is of the opinion that, through reasonable charges to physicians going through the program and to hospitals that receive assurance regarding the medical qualifications of their foreign-trained house staff as a result of this evaluation service, the program can ultimately become self-supporting.

The Council on Medical Education and Hospitals, through its representatives on the Cooperating Committee on Graduates of Foreign Medical Schools and from reports, has been constantly informed of the work of the Cooperating Committee. On the basis of full knowledge and careful study of the planning of the Cooperating Committee, the Council on Medical Education and Hospitals enthusiastically supports this proposed program in the belief that it provides a sound and effective mechanism not otherwise available for evaluating the medical qualifications of foreign-trained physicians coming to the United States. It is recommended that the House of Delegates approve in principle the program proposed in this report.

Respectfully submitted,

H. G. WEISKOTTEN, Chairman
GUY A. CALDWELL.
HARLAN ENGLISH.
VICTOR JOHNSON.
FRANKLIN D. MURPHY.
W. ANDREW BUNTEN.
JOHN W. CLINE.
JAMES M. FAULKNER.
LELAND S. MCKITTRICK.
CHARLES T. STONE.
EDWARD L. TURNER, Secretary

THE JOURNAL INDEX

The index to volume 160 of THE JOURNAL appears in this issue. Those who wish extra copies of the index may receive them without charge on request to the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

TELEVISION

The American Medical Association will continue to cooperate with Ciba Pharmaceutical Products, Inc., in presenting "Medical Horizons" next season. Beginning Sunday, Sept. 9, the half-hour documentaries will be seen at 4:30 p. m. EDT each Sunday on the American Broadcasting Company television network. Eighty-five stations, twice as many as last year, will carry the program. T. Davies Haines, president of Ciba, commenting on the new series, said, "We trust that the greatly expanded coverage and continuity of the series will inspire increased confidence in the American medical profession. We plan to have programs on advances in common everyday problems in medicine as well as on major diseases which as yet have not been fully conquered." The format of the "Medical Horizons" show will remain the same. Don Goddard, veteran newscaster, will return as host-narrator and Dr. William T. Strauss of Ciba will continue as medical supervisor.

FORD FOUNDATION MATCHES MEDICAL EDUCATION GRANTS

H. Rowan Gaither Jr., president of the Ford Foundation, announced on April 15 a 10 million dollar program of matching grants to the National Fund for Medical Education. Mr. Gaither said the Ford Foundation grants will be made on a matching basis over a 5-to-10-year period with a maximum grant in any one year limited to 2 million dollars. All contributions in 1956 in excess of the 1955 total of $2,147,000 would be matched dollar for dollar, subject to the annual maximum of 2 million dollars.

After 1956, each year's grant would match the preceding year's receipts on a diminishing scale, but all receipts over the preceding year's total would be matched dollar for dollar, up to the 2 million dollar annual ceiling. The announcement of these matching grants will mean that, for every unearmarked dollar contributed to A. M. E. F., another 70 cents to a dollar will be given by the Ford Foundation, thereby stimulating additional financial support that the nation's medical schools have so critically needed.

This new appropriation is totally distinct from the 90 million dollar (endowment) appropriation announced by the Ford Foundation in December that will be paid directly to the schools after consultation with an advisory group still to be formed.

DRS. MURRAY AND MARTIN HONORED

President-Elect Dwight H. Murray was one of two persons who received a "Dignity of Man" award given by the Kessler Institute for Rehabilitation at a civic banquet at West Orange, N. J., on April 11. Dr. Murray received his award for his "unique contribution" as a leader in American medicine. The banquet, attended by 400 civic leaders in and around West Orange, also was the occasion for celebrating the 60th birthday anniversary of Dr. Henry H. Kessler, who was one of the founding members of the A. M. A. Council on Industrial Health.

The Medical College of Virginia has announced that it would confer an honorary degree of doctor of science on past-president of the A. M. A., Dr. Walter B. Martin, at the commencement exercises, May 29. Also receiving an honorary degree at the same commencement will be Dr. William Ramsey Laird, chief surgeon of the Laird Memorial Hospital in Montgomery, W. Va. He will receive a doctor of literature degree. Dr. Laird is a member of the Board of Governors of the American College of Surgeons.

FEDERAL MEDICAL LEGISLATION

Second Session, 84th Congress

Bureau of Older Persons

Congressmen Yates (D., Ill.), in H. R. 8863, Green (D., Ore.), in H. R. 8941, Reuss (D., Wis.), in H. R. 9092, and Ashley (D., Ohio), in H. R. 9168, have introduced identical measures to provide for the establishment of a bureau of older persons in the Department of Health, Education, and Welfare and to authorize federal grants to assist in the development and operation of studies and projects to help older people. The states would be required to designate a state officer or agency for developing state plans. Grants would be made to the states with the federal government contributing between one-third and two-thirds of the cost of the projects. Authorization of 2 million dollars would be made to the states to develop their plans. The grants thereafter for the cost of the projects would be 2 million dollars for the fiscal year 1958, 3 million dollars for the fiscal year 1959, 4 million dollars for the fiscal year 1960, and 5 million dollars for the fiscal year 1961. An advisory committee on aging and geriatrics would be authorized. These measures were referred to the Committee on Education and Labor.

Mosquito Research and Control Grants

A group of identical bills have been introduced to provide for mosquito research and control grants. The earliest bill, S. 2870, was previously reported. The new bills are by Congressmen Thompson (D., La.), in H. R. 8921, Willis (D., La.), in H. R. 8923, Brooks (D., Texas), in H. R. 8892, and Metcalf (D., Mont.), in H. R. 9273. These bills were referred to the Interstate and Foreign Commerce Committee.

Water Pollution Control

Representative Bailey (D., W. Va.), in H. R. 8885, would extend the duration of the Water Pollution Control Act through June 30, 1966, and authorize the appropriation of a sum not to exceed 100 million dollars for the complete period. This bill would also authorize the federal government to lend up to two-thirds of the project cost of construction and treatment works for sewage or other waste discharged into streams. The limit of federal loans would be increased from $250,000 to $1,000,000 for a single project. This measure was referred to the Committee on Public Works.

Medical-Dental Research and School Construction

Congressmen Priest (D., Tenn.), in H. R. 9013, and Wolverton (R., N. J.), in H. R. 9014, and Senator Purtell (R., Conn.), for himself, and Senators Smith (R., N. J.), Bridges (R., N. H.), Ives (R., N. Y.), Allott (R., Colo.), Bender (R., Ohio), and Bennett (R., Utah), in S. 3252, have introduced identical measures to authorize a five-year program of federal construction grants to assist medical and dental schools in expanding and improving their research and teaching facilities and to assist other public and nonprofit institutions engaged in medical or dental research to expand and improve their research facilities. Annual appropriations would be authorized not to exceed 250 million dollars beginning July 1, 1956, and ending June 30, 1961. Of this, 210 million dollars would be authorized for medical research and teaching facilities and 40 million dollars for dental research and teaching facilities. Schools of medicine, osteopathy, public health and dentistry, universities, and other public and nonprofit educational institutions, laboratories, and research institutions would be eligible for grants. No institutions would be eligible for a grant for a project that could be obtained under the Hospital and Survey Construction Act (Hill-Burton) except as a surgeon general specifically determined that a particular project was designed for and intended to be used for research and teaching. Grants could not exceed 50% of the necessary cost of the construction. A national advisory council on medical research and teaching facilities would be authorized. The House bills were referred to the Interstate and Foreign Commerce Committee and the Senate bill to the Committee on Labor and Public Welfare.

Mental Health Study Grants

Congressman Priest (D., Tenn.), in H. R. 9048, and Senator Hill (D., Ala.), in S. 3138, would amend the Public Health Service Act to broaden the authority of the surgeon general in making grants to states or local agencies, universities, laboratories, and other public or private agencies and to individuals for investigations, experiments, demonstrations, and research projects with respect to the development of improved methods of diagnosing mental illness and of care, treatment, and rehabilitation of the mentally ill. The House measure was referred to the Interstate and Foreign Commerce Committee and the Senate measure to the Committee on Labor and Public Welfare.

Medical and Dental Officer Procurement

Senators Russell (D., Ga.) and Saltonstall (R., Mass.), in S. 3123, have introduced an identical measure with H. R. 8500, which was previously reported, to improve the medical procurement procedures and incentives for medical and dental officers for the uniformed services. This measure was referred to the Senate Armed Services Committee.

Transfer of Allotments in Hospital Construction

Senators Malone (R., Nev.) and Bible (D., Nev.), in S. 3130, and Congressman Young (R., Nev.), in H. R. 9227, have introduced measures to allow states with a population of fewer than 700,000, according to the 1950 census, to transfer 50% of the unused portions of categorical grants from one category to another under the Hospital Construction Act, if it could be shown that lapsed funds for one category of projects existed because no approvable applications for funds were pending. At present, allotments are made for each of the following categories: (1) construction of general hospitals; (2) diagnostic or treatment centers; (3) hospitals for the chronically ill; and (4) rehabilitation facilities and nursing homes. The Senate bill was referred to the Committee on Labor and Public Welfare. The House bill was referred to the Committee on Interstate and Foreign Commerce.

Prepared by the Washington Office of the American Medical Association.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

NOTES FROM THE COUNCIL

University of Miami School of Medicine Approved

At its meeting in Boston, Nov. 27-28, 1955, the Council on Medical Education and Hospitals voted approval of the University of Miami School of Medicine, which will graduate its first class in June, 1956, and authorized that the institution be included in the next listing of approved medical schools in the 1956 education issue of THE JOURNAL, the action being contingent upon similar action by the Executive Council of the Association of American Medical Colleges. On Feb. 10, 1956, the Liaison Committee on Medical Education representing the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges reported the approval of the school and concurred in its listing by the Council on Medical Education and Hospitals and its admission to membership by the Association of American Medical Colleges. Due to its continuing developmental status, the school will be revisited by a liaison group representing the two Councils during the next (1956-1957) academic session.

Action on Other Medical Schools Visited by Liaison Survey Groups

Liaison groups representing the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Asssociation of American Medical Colleges visited the medical schools listed below since the last meeting of the Committee and submitted formal reports of their findings and recommendations. Both Councils and the Liaison Committee on Medical Education concurred in their continued listing of the following schools as approved schools of medicine: University of South Dakota, visited Oct. 31-Nov. 2, 1955; University of Maryland, visited Nov. 14-16, 1955; Tulane University, visited Dec. 12-15, 1955; Jefferson Medical College, visited Jan. 9-12, 1956; and University of Nebraska, visited Jan. 23-25, 1956.

Annual Liaison Visits to Newly Developing Medical Schools

For many years it has been the policy of the Council on Medical Education and Hospitals of the American Medical Association and the Executive Council of the Association of American Medical Colleges to withhold formal inspection and action on a newly developing medical school until all of its contemplated four-year program was organized and in operation. Discussion of this procedure by both Councils independently and later by the Liaison Committee on Medical Education indicated that it would be distinctly advantageous to a newly developing medical school to have a liaison survey when the first two years have been organized and in full operation and a complete survey again when the full four-year program is in operation. Both Councils concurred and in December of 1954 the Liaison Committee on Medical Education voted to grant provisional approval to newly developing medical schools on the completion of two years of organization and operation if conditions upon evaluation warrant such recognition.

Subsequently, at its meeting on Oct. 23, 1955, at Swampscott, Mass., the Liaison Committee recommended that in addition it would be advantageous to all concerned if such institutions were visited annually and advised whether they were proceeding in a manner that would meet standards for accreditation. Both Councils have subsequently voted to approve the recommendations of the Liaison Committee and have now established the policy of visiting newly developing medical schools annually. Since both the University of Missouri and the University of Mississippi have organized their third-year programs and have them in operation, these two institutions are being included in the medical school liaison visitation schedule prior to the end of the current (1955-1956) academic year.

Advisory Committee on Postgraduate Medical Education

After careful consideration of an extensive résumé on postgraduate medical education prepared by the staff, the Council on Medical Education and Hospitals at its meeting on Feb. 9-10, 1956, approved the appointment of an Advisory Committee on Postgraduate Medical Education. This committee is to be selected from organizations and groups, so that broad representation of the varying needs and points of view can be as adequately represented as possible. Some of the questions that this committee will be asked to consider include:

1. What should be the broad objectives of postgraduate medical education?
2. What should be the over-all objectives and role of the Council in this field?
3. Should the Council emphasize postgraduate opportunities for general practitioners? If so, in what way?
4. Should the Council prepare and publish "guides" (rather than "essentials") with an emphasis on flexibility for those desiring to improve or initiate postgraduate programs?
5. Should the Council continue to prepare listings of programs that are not evaluated in any sense other than by the statement of the sponsor for publication in THE JOURNAL?
6. How might reasonable evaluations be made of the many programs now being offered?
7. Should any form of accreditation of postgraduate offerings be considered?
8. Should the Council encourage an attitude favoring regionalization of postgraduate programs among medical schools and hospitals?
9. How can the Council best aid in encouraging continuing education in the medical profession?
10. In what ways might the American Medical Association and the Council on Medical Education and Hospitals aid in greater utilization of the increasingly valuable audio-visual adjuncts and aids in the promotion of regional and national postgraduate medical education?

COUNCIL ON MEDICAL SERVICE

AGREEMENT BETWEEN MINERS FUND AND PENNSYLVANIA MEDICAL SOCIETY

At its recent meeting in Detroit on Jan. 23, 1956, the Committee on Medical Care for Industrial Workers, a joint committee of the Council on Medical Service and the Council on Industrial Health, reviewed some of the progress made during the past few years in improving relationships between the medical profession and the Welfare and Retirement Fund of the United Mine Workers of America in an effort to improve medical care.

Three annual conferences on Medical Care in the Bituminous Coal Mine Areas, sponsored by the Committee, have made important strides in bringing about greater understanding between the union and the medical societies in the areas involved. At its most recent conference in Huntington, W. Va., in October, 1954, the Committee on Medical Care for Industrial Workers observed that, "The Conference was in general agreement that progress in solving problems has been achieved but that more work is necessary." As the Council on Medical Service stated in its report to the House of Delegates at the Clinical Session in Boston, "The air of general satisfaction that had permeated the conference was shattered, however, with the issuance of a directive from area medical administrators in the Spring of this year (1955) that severely restricted the practice of the general practitioner and imposed specialist consultation requirements that did not previously exist. Medical societies in the coal mining area reacted immediately and unfavorably to the new directive and passed resolutions condemning it."

After considering the four resolutions condemning this directive, the Reference Committee on Insurance and Medical Service recommended adoption of the following resolution, which was then adopted by the House of Delegates at its June meeting in Atlantic City.

RESOLVED, That the House of Delegates of the American Medical Association expresses its disapproval of that portion of the directive issued by the executive medical officer of the U. M. W. A. Welfare and Retirement Fund which requires consultation by a specialist before admission to a hospital of all beneficiaries of this program who are treated by physicians other than those approved by the U. M. W. A. Welfare and Retirement Fund as specialists; and be it further

RESOLVED, That all other controversial matters arising between the U. M. W. A. Welfare and Retirement Fund and the participating physicians which cannot be reconciled at the local or state level shall be promptly referred to the Committee on Medical Care for Industrial Workers of the Council on Medical Service and the Council on Industrial Health of the American Medical Association.

On Sept. 21, 1955, the executive medical officer of the United Mine Workers Welfare and Retirement Fund, in his address before the 105th annual session of the Medical Society of the State of Pennsylvania in Pittsburgh, withdrew the directive. This action prompted the committee on medical economics of the state medical society to invite him to a series of meetings in an effort to resolve amicably existing problems and to establish a procedure whereby current and future grievances and problems might be adequately dealt with. The following agreement is the result of these deliberations. It contains principles of procedure and a method of resolving problems and disputes that deserve the attention of the medical profession in general, third party mechanisms providing medical care services, and state societies in particular.

The agreement as printed below should not be viewed as a rigid and inflexible document to be adopted *in toto* by other societies. It is, rather, an example of how other understandings can be arrived at based upon local conditions and situations. The Committee on Medical Care for Industrial Workers believes that this is another "heartening example" of objectives that can be achieved where statesmanship and understanding join in common effort and resolve to promote the best interests of the public and those of the medical profession in providing medical care of the highest quality.

AGREEMENT

Between The Medical Service, U. M. W. A. Welfare and Retirement Fund and the Medical Society of the State of Pennsylvania.

Although the principles enunciated herein indicate, by phraseology, that they are applicable in the relationship between the United Mine Workers of America Welfare and Retirement Fund and the medical profession in Pennsylvania, it is recommended by the State Society that these principles shall also be applicable in its relationship to other groups in situations comparable to those pertaining to the Fund.

It is agreed that in those cases where the Fund desires to make changes in basic procedure or policy in the operation of the Fund, such proposals will be initially presented at the State Level to the Committee on Medical Economics. Under such provision the Area Medical Administrators would present the matter to the Committee on Medical Economics with their reasons for the action contemplated. The Committee might either state its position forthwith,* or defer action pending referral to the District and County Liaison Committees for expression of their views. Consideration at appropriate levels would thereby be assured, and the final action taken at the state committee level would reflect the judgment of all, based upon full knowledge of the facts and the reasons for the changes contemplated. An added advantage would be the opportunity for alternate proposals which such procedure would afford. In the event that agreement with the Medical Service of the Fund could not be reached at the state committee level, a summary of the most essential facts developed in the course of this procedure, with the arguments for and against the changes under consideration, would greatly facilitate the deliberations of the Committee on Medical Care for Industrial Workers of the Council on Medical Service and the Council on Industrial Health of the A. M. A. to which the matter would then be referred.

It is agreed that The Medical Society of The State of Pennsylvania will recommend that in those hospitals where committees dealing with medical or surgical audits already exist, these functions be expanded to the status of full Medical Audit Committees** to include the evaluation of the quality of medical service provided in all departments of the hospital; the review of hospital admissions and length of stay, including their necessity; the necessity of procedures carried out; the general adequacy of patient care including medically indicated consultations or referrals. These functions may be carried out by the Committee as a whole or by subcommittee groups assigned to special functions. In those hospitals not having Medical Audit Committees, it is recommended that a committee with the aforementioned functions be formed as soon as practicable.

It is agreed that it is the duty of all physicians, including those employed by the Fund, to expose incompetent, corrupt, dishonest or unethical conduct on the part of members of the profession.

* Note: [This would be done] after receiving approval by the Board of Trustees of The Medical Society of the State of Pennsylvania through which the committee must work because of its status as a fact-finding committee only. Immediate decisions by the Committee on Medical Economics would depend on previously decided policies, with changes in policies requiring approval by the Board of Trustees.

** Reference: Recommendations of the Joint Commission on Hospital Accreditation.

In such instances members may be "charged" with violation of the *Principles of Medical Ethics.*

Organized medicine does not concede to a third party the prerogative of passing judgment on the treatment rendered by physicians including the necessity of hospitalization, length of stay and the like. It is the responsibility of organized medicine to take the initiative in searching out abuses and instituting measures for their correction. The Medical Service of the Fund shall cooperate wholeheartedly in providing information to the proper committees of Hospital Staffs and Liaison Committees at local and higher levels to aid in the solution of [such] difficulties. . . .

We mutually endorse the basic principle that all qualified physicians be granted appropriate hospital staff privileges in order to insure adequate medical care for the community. We also recognize that it is the prerogative of the individual hospital governing board to make final decisions on applications for staff membership.

It is agreed that any physician who wishes to be included in the list of Participating Physicians shall apply to the Area Medical Administrator, giving his qualifications and stating the category in which he desires to be listed. Such application shall be sent to the Area Medical Administrator with an informational copy to the County Liaison Committee. In the event that his application does not receive favorable action, he may appeal to the County Liaison Committee, which will deal with the matter according to procedure outlined later in these agreements. In those cases reviewed by the Liaison groups, decisions recommending that a physician should be listed shall include the special category, if any, in which the Liaison group feels the individual should be listed. Such recommendations shall be accompanied by adequate and valid supporting data.

It is agreed that the general format of the Participating List be of the type now printed by the Pittsburgh Area Medical Office, namely, the issue of April 15, 1955. It is also agreed that each listed physician . . . be specifically designated either as a specialist, a general practitioner, or other appropriate designation.

It is agreed that the number of beneficiaries, however small, treated by a physician, will not in itself be considered as a justifiable cause for removing a physician from the participating list. It is also agreed that in addition to violation of the Principles of Medical Ethics, such procedures as unnecessary hospitalization, undue length of stay, unnecessary surgery, services of an inferior quality, and the like, shall be justifiable cause for removing a physician from the list. Those grieved by such action shall have the right to appeal through the Liaison Procedure.

The Medical Society of The State of Pennsylvania, in order to insure a high standard of medical care, as determined by Medical Audit Committees,* agree to adequate consultation after hospital admission. Further consultation, either before or after hospital admission, is a third party prerogative for just cause such as—recurrent admissions, repeated referrals, prolonged medical care, and excessive hospital stay.

Temporarily it is agreed that each individual physician shall have the right of decision as to the method of payment for his services without jeopardizing his relationship with the Fund. It is also agreed that since many physicians believe that the fee-for-service method of payment is the type of payment most conducive to good medical care, and since the A. M. A. Judicial Council is presently reviewing methods of payment for physicians' services, that this matter remain "open" and subject to later amendment. It is agreed that the Board of Trustees of The Medical Society of The State of Pennsylvania will take the necessary action to bring about an expeditious decision regarding this subject from the A. M. A. Judicial Council.

Should either party become dissatisfied with this agreement, in whole or in part, he shall request a meeting with the other party to discuss points of difference. Such meeting shall be held within 30 days of the request. If the points of difference cannot be resolved, then that portion of this agreement affected thereby, shall be considered inoperative until such differences are resolved to the satisfaction of both parties.

It is agreed that the Liaison Procedure outlined . . . shall become a part of this agreement.

This agreement shall be effective on January 16, 1956.

Adopted by The Board of Trustees of The Medical Society of The State of Pennsylvania on November 17, 1955.

LIAISON PROCEDURE

1. The Area Medical Administrator, individual physicians, hospital staffs and other local groups should make every effort to reach a satisfactory agreement on controversial matters. . . .

The Fund maintains the right to suspend individuals temporarily for cause.

When a satisfactory solution cannot be reached, or in case of the temporary suspension of a physician from the participating list, either party shall have the right of appeal to the:

a) *County Medical Society Liaison Committee.* This committee shall render an advisory opinion within 60 days, unless for valid reasons, agreeable to both parties, a time extension is thought to be necessary. If necessary, the judicial body to receive the deliberations of the Liaison Committee shall be the County Society Board of Censors. If no satisfactory solution is reached then either party shall have the right to appeal to the:

b) *District Liaison Committee.* This committee shall render an advisory opinion within 30 days, unless for valid reasons, agreeable to both parties, a time extension is thought to be necessary. If necessary, the judicial body to receive the deliberations of the District Liaison Committee shall be the District Board of Censors. The District Liaison Committee shall be composed of the District Councilor and Trustee as chairman, and the chairmen of each county medical society Liaison Committee in the respective district. If no satisfactory solution is reached then either party shall have the right to appeal to the:

c) *Committee on Medical Economics of The Medical Society of The State of Pennsylvania.* This committee shall render an advisory opinion within 30 days, unless for valid reason, agreeable to both parties, a time extension is thought to be necessary. If necessary, the judicial body to receive the deliberations of the Committee on Medical Economics shall be the Board of Trustees of The Medical Society of The State of Pennsylvania sitting in Judicial Council. If no satisfactory solution is reached, then either party shall have the right to appeal through appropriate channels, to the American Medical Association, Committee on Medical Care for Industrial Workers.

d) In all cases appealed to a higher echelon, informatory copies of the actions taken and/or charges made shall be forwarded to the next higher echelon of liaison by the Area Medical Administrator, the individual physician, or the liaison group taking the action and/or filing the charges.

2. When changes in basic procedure are involved, the Area Medical Administrators concerned will present the matter to the Committee on Medical Economics of The Medical Society of The State of Pennsylvania with their reasons for the action contemplated. The Committee will either state its position forthwith (Board approval may be necessary) or defer action for not longer than 30 days, pending referral to the District and County Liaison Committees for expression of their views.

In the event that agreement with the Medical Service of the Fund cannot be reached at the state committee level, a summary of the essential facts developed in the course of this procedure, with the arguments for and against the changes under consideration will greatly facilitate the deliberations of the A. M. A. Committee of the Council on Medical Service and Council on Industrial Health to which the matter would then be referred.

3. The Medical Society of The State of Pennsylvania will recommend to the county medical societies that each county medical society liaison committee consist of three or five physicians on a revolving membership basis, with each physician serving for a period of three or five years, with the senior member acting as chairman. The chairman of the county medical society liaison committee will also serve as a member of the District Liaison Committee. One member will be designated as secretary and accurate records of meetings will be kept on file. The county medical society will, on the basis of the size of its total membership, determine whether the committee should consist of three or five members. The Medical Society of The State of Pennsylvania will recommend that all county medical society liaison committees be *elected* by the county medical society as a whole rather than be chosen by appointment.

* Note: When such Medical Audit Committees are found to be functioning properly, the Fund will no longer find it necessary to require routine consultation after Hospital admission.

MEDICAL NEWS

FLORIDA

Seminar on Diagnosis and Therapy.—The Mount Sinai Hospital of Greater Miami announces the sixth annual postgraduate seminar on "Recent Advances in Diagnosis and Therapy" at the Fontainebleau Hotel, Miami Beach, May 17-20. The lecturers will be Drs. Alexander Brunschwig, Louis Leiter, and Solomon Silver, New York; Dr. Joseph J. Bunim, Bethesda, Md.; Dr. George Crile Jr., Cleveland; Dr. Robert B. Greenblatt, Augusta, Ga.; Dr. Keith S. Grimson, Durham, N. C.; Dr. William F. Rienhoff Jr., Baltimore; Dr. Hans Selye, Montreal, Canada; and Dr. Edward Weiss, Philadelphia. The fee, $20, may be mailed to the Seminar Committee, Mount Sinai Hospital of Greater Miami, Miami Beach.

ILLINOIS

County Society Public Relations Day.—The annual public relations meeting day of the Adams County Medical Society will be observed in Quincy May 14. The meeting will be open to physicians and dentists and their assistants and secretaries, pharmacists, nurses, technicians, public health personnel, hospital administrators, record clerks and trustees, and medical society auxiliary members of the Quincy tristate area. A fellowship hour, 7 p. m. at the Lincoln Douglas Hotel, will precede a talk by Mr. Leo E. Brown, Chicago, Director of Public Relations of the American Medical Association. The talk will be followed by a complimentary snack bar lunch.

Anesthesiologists Meet in Chicago.—The Illinois Society of Anesthesiologists will hold its annual meeting May 13 at the Hotel Sherman, Chicago. The following program will be presented at 10 a. m.:

Office Anesthesia, Hugh O. Brown, Salt Lake City.

Management of Anesthesia in Patients with Pulmonary Emphysema, Karl L. Siebecker, Madison, Wis.

Fundamental Pharmacology in Relation to Anesthesia, John Adriani, New Orleans.

Postoperative Vomiting, Fact and Fancy, Edward C. Mayer, Evanston.

After a round-table luncheon, "Cardiac Resuscitation, Panic or Purpose" will be discussed at 2 p. m. by Col. Harvey C. Slocum, M. C., consultant in anesthesiology, Office of the Surgeon General, Department of the Army.

Meeting of Surgical Society.—The annual meeting of the Illinois Surgical Society will be held May 14 in Chicago. Surgical clinics will be at 8 a. m. at the Cook County Hospital (Harrison and Wood streets). The program includes a panel symposium on surgery of the colon and demonstrations of "Production and Resuscitation of Cardiac Arrest" and "The Care of the Severely Burned Patient." The scientific meeting is scheduled for 5:30 p. m. at the University Club (Michigan Avenue and Monroe Street), where the following program will be presented:

Persistence of Symptoms Following Cholecystectomy, Waltman Walters, Rochester, Minn.

Duodenal Ulcer, Hypothalamus, Pituitary, Adrenal Axis, Lester R. Dragstedt, Chicago.

Thoracic Surgery by the General Surgeon, Jerome R. Head, Chicago.

Dinner reservations for members and guests may be made through Dr. William M. McMillan, 122 S. Michigan Ave., Chicago 3 (HArrison 7-5065). The medical profession is invited to all sessions.

State Medical Meeting in Chicago.—The 116th annual meeting of the Illinois State Medical Society will convene May 15-18 at the Hotel Sherman, Chicago, under the presidency of Dr. F. Garm Norbury, Jacksonville, who will open the general assembly Tuesday at 1:30 p. m. The following program will then be presented:

Roentgen Evaluation of the Chest, Chester H. Warfield, Fort Wayne, Ind.

Urinary Incontinence in the Female, John C. Ullery, Columbus, Ohio.

Anesthetic Consideration in the Acutely Injured Patient, Harvey C. Slocum, Washington, D. C.

Acute Coronary Occlusion Reconsidered, E. Grey Dimond, Kansas City, Kan.

Gamma Globulin in Disease, Robert A. Good, Minneapolis.

Physiology of Transient Loss of Vision, Henry P. Wagener, Rochester, Minn.

A public relations dinner has been scheduled by the committee on medical service and public relations for Tuesday evening, and a program and buffet supper will be given by the woman's auxiliary Tuesday at 9 p. m. The president's address, "Medicine: An Art and a Science," Wednesday, 1:30 p. m., will be followed by the oration in surgery, "The Functional Nature and Clinical Significance of Some Thyroid Tumors," by Dr. Brown M. Dobyns, Cleveland, and the oration in medicine, "Streptococcal Infection, Rheumatic Fever, and Nephritis," by Dr. Charles H. Rammelkamp, Cleveland. At 3:10 p. m. there will be a symposium on prevention and treatment of automobile accidents in which Sgt. Elmer C. Paul, supervisor, Auto Crash Injury Research Section, Indiana State Police, Indianapolis, will give a brief review of "The Auto Crash Injury Research Program" and will then present "Causes of Occupant Injuries." "The Search," a film showing the results of the Cornell University research division on crash injuries and results of field and laboratory studies, will be shown. Dr. Walter J. R. Camp, Chicago, will discuss "Drivers, Drinks and Drugs"; Dr. Wayne B. Slaughter, Chicago, "The Immediate Care of Maxillofacial Injuries"; and Dr. Willard M. Easton, Peoria, "Injuries of the Lower Urinary Tract." Dr. Arkell M. Vaughn, Chicago, immediate past-president, will serve as toastmaster at the annual dinner Wednesday, 7 p. m., at which the guest speaker, Dr. Elmer Hess, Erie, Pa., President of the American Medical Association, will present "The Human Side of Medicine." The section on obstetrics and gynecology has a panel discussion, "Obstetrical Hemorrhage," for Tuesday, 10:30 a. m., and the section on radiology a film reading session for Tuesday afternoon. At a joint meeting with the section on medicine Wednesday morning, the section on pediatrics will hold a symposium on the use of steroids. The section on eye, ear, nose, and throat will devote its Wednesday morning session to a symposium, "Neurologic Complications of Eye, Ear, Nose and Throat," and a panel, "Clinical Aspects of Neuralgia of the Head." Wednesday at 10:30 a. m., the section on surgery will have a panel discussion on gallbladder diseases. Thursday morning the section on pediatrics will present a symposium on antibiotics and the section on dermatology a symposium on the management of common skin diseases and a panel, "The Management of the Scaling Eruptions." On Friday morning the section on pathology will hold a panel discussion, "Methods of Forensic Pathology for the General Pathologist." The woman's auxiliary will meet simultaneously.

Chicago

Moorhead Memorial Lectureship.—On May 16, the Stritch School of Medicine of Loyola University and Phi Beta Pi Fraternity will present the annual L. D. Moorhead Memorial Lectureship, "The Changing Scene in Anesthesia," by Dr. Max S. Sadove, chairman, division of anesthesiology, University of Illinois College of Medicine. The lecture, which will be delivered at 8 p. m. in the amphitheatre of the Loyola University School of Dentistry, 1757 W. Harrison St., is open to all.

Lectures on Growth of Medicine.—In its series of lectures on the growth of medicine (Wednesdays, 5-6 p. m., in Thorne Hall), Northwestern University Medical School on May 16 will present Dr. Eugene M. K. Geiling, professor of pharmacology, University of Chicago School of Medicine, who will have as his

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

subject "John Jacob Abel," and on May 23 Dr. Joseph A. Capps, clinical professor emeritus, University of Chicago Medical School, whose subject will be "Frank Billings."

Alumni Banquet.—The Medical Alumni Association, University of Illinois College of Medicine, will hold its annual banquet (informal) May 14 in the Walnut Room at the Bismarck Hotel (Randolph and Wells streets). Guests are invited. Cocktails at 6 p. m. will precede dinner at 7 p. m. Reunions will be held for the classes of 1901, 1906, 1911, 1916, 1921, 1926, 1931, 1936, 1941, and 1946. Check for reservations ($7.50 a plate) should be sent to Mrs. Michael H. Streicher, Honorary Executive Secretary, Medical Alumni Association, 415 Fullerton Pkwy., Chicago 14.

Faculty-Alumni Reunion Dinner.—The Northwestern University Medical Annual Faculty-Alumni Reunion dinner will be held May 12 at the Furniture Club of America, 666 Lake Shore Dr. Couples are invited to attend the social period, 6 p. m., and the dinner at 7 p. m. The traditional musical entertainment, "Quo Vadis Medicus? '56. Operation Osculation," will be presented by medical students. Tickets for the dinner ($8 each) may be obtained at the Medical Alumni Office, 303 E. Chicago Ave., Chicago 11. Special tables will be reserved for the reunion classes: 1901, 1906, 1911, 1916, 1921, 1926, 1931, 1936, 1941, 1946, and 1951.

Joint Meeting on Ophthalmology.—A joint open meeting of the Institute of Medicine of Chicago and the Chicago Ophthalmological Society will be held in the Drake Hotel at 8 p. m., May 14. Dr. Bernard Becker, head, department of ophthalmology, Washington University School of Medicine, St. Louis, will deliver the second Edward Lorenzo Holmes Memorial Lecture of the Institute of Medicine of Chicago, "The Rate of Secretion of Aqueous Humor," and the Edward Lorenzo Holmes citation and award will be presented to him. All are welcome. Telephone during the meeting, SUperior 7-2200. Cocktails, 6 p. m., will be followed by dinner, 6:45 p. m. ($6 per plate). Reservations may be made through the Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1.

MARYLAND

Symposium on General Practice.—On May 17 a Symposium on General Practice will be held at the Sheraton-Belvedere Hotel, Baltimore, under the joint auspices of the Maryland and District of Columbia chapters of the American Academy of General Practice and the sponsorship of Lederle Laboratories. The following program will be presented at 9:30 a. m.:

Use of Steroids in General Practice, William Dock, Brooklyn.
Modern Concepts of Prenatal Care, Edwin J. DeCosta, Chicago.
Coronary Occlusion: Management of Acute and Convalescent Stages, Robert L. Parker, Rochester, Minn. (tentative).
Application of Physical Medicine in General Practice, Donald A. Covalt, New York.
Office Surgical Procedures for the General Practitioner, Ben Eiseman, Denver.
Management of Jaundice (lecturer unannounced).

At noon, members of the academy will be the guests of Lederle Laboratories at a luncheon, for which the speaker will be Norman Cousins, editor of the *Saturday Review of Literature*.

MICHIGAN

Lecture on Smoking and Lung Cancer.—On May 15 at 8:15 p. m. the Henry Ford Hospital Medical Society will present in the Henry Ford Hospital Auditorium, Detroit, the Roy D. McClure Memorial Lecture, "How Good Is the Evidence for an Etiological Relationship Between Cigarette Smoking and Cancer of the Lung?" by Dr. Evarts A. Graham, professor of surgery, Washington University School of Medicine, St. Louis.

MONTANA

Society News.—Dr. Chester W. Lawson, Havre, chairman, maternal and child welfare committee, Montana Medical Association, announces the availability of a program on erythroblastosis and exchange transfusions, arranged by the committee, which will be glad to present it, on request, at a scientific meeting of any component society of the association.——The Montana Society of Medical Technologists will hold its annual convention May 18-19 in Great Falls at the Meadow Lark Country Club. An invitation is extended to all members of the Montana Medical Association and their technologists to attend. Dr. Tyra T. Hutchens, associate professor of pathology, University of Oregon Medical School, Portland, will discuss radioisotopes and medical technology and the laboratory evaluation of thyroid functional status. Mr. Glen Hill, director, division of serologic development, Ortho Research Foundation, Raritan, N. J., will discuss the developments in Rh typing and cross matching techniques.

NEBRASKA

State Medical Meeting in Lincoln.—The 88th annual session of the Nebraska State Medical Association will convene May 14-17 at the Hotel Cornhusker, Lincoln. The presidential address by Dr. William E. Wright, Creighton, Tuesday, 2:30 p. m., will precede the installation of the incoming president, Dr. James M. Woodward, Lincoln. Presentations by out-of-state speakers will include:

Problem of Heart Disease in Pregnancy, James E. Fitzgerald, Chicago.
Hazards of Multiparity, G. Keith Folger, Cleveland.
Hemorrhagic Diathesis in Pregnancy, Oscar D. Ratnoff, Cleveland.
On Medical Writing, Jacques P. Gray, Detroit.
Experimental Psychoses Which Mimic Schizophrenia, Howard D. Fabing, Cincinnati.
Bladder Neck Obstruction in Adult Males, Edgar Burns, New Orleans.
Basic Management of Hemiplegics, Jack K. Wickstrom, New Orleans.
Clinical Problems in Fluid and Electrolyte Balance in the Aged, C. Thorpe Ray, New Orleans.
Controlled Deceleration in the Automobile, Horace E. Campbell, Denver.
Trauma of Childhood, Vernon C. Turner, Evanston, Ill.
Management of Fractures of the Hip, Robert T. McElvenny, Chicago.
Ununited Fractures of the Carponavicular, James K. Stack, Chicago.

A symposium, "Medical Complications During Pregnancy," is scheduled for 3:30 p. m. Tuesday, at which time there will also be a seminar on medical writing. The Wednesday afternoon session will open with a round table, "The Confusion States," and the Thursday afternoon session with a symposium, "Trauma to the Skeletal System," which will include presentations by Drs. Hampar Kelikian, Chicago, and Howard W. Schneider, Harvey, Ill. Fun night is scheduled for 6:30 p. m. Tuesday. A social hour at 6 p. m. Wednesday will honor the president and the president of the women's auxiliary, which will meet concurrently. At the annual banquet Wednesday, 7 p. m., the speaker will be Mr. Samuel C. Waugh, president, Export-Import Bank, Washington, D. C., who will have as his subject, "A Country Boy Goes to Washington." There will be a sportman's dinner at the Lincoln Country Club, Monday, 7 p. m., a golf tournament at that club at 12:30 p. m., and a trap shoot at the Lincoln Gun Club at 1 p. m.

NEW JERSEY

State Medical Meeting in Atlantic City.—The Medical Society of New Jersey will hold its 190th annual meeting at Haddon Hall, Atlantic City, May 12-16. A civil defense symposium on emergency medical and surgical treatment in disaster has been planned for Sunday, 8 p. m. The program will include two panel presentations by surgeons and a round-table panel discussion. Dr. Vincent P. Butler, Jersey City, president, will preside at the general session Monday, 8:30 p. m., at which Dr. Lewis C. Fritts, Somerville, president-elect, will deliver his inaugural address. A dinner-dance honoring President and Mrs. Butler will be held Tuesday evening. The section on clinical pathology will have as guest speaker Tuesday, 10 a. m., Dr. Emma S. Moss, New Orleans, whose presentation on "The Mycoses" will precede a symposium, for which she will serve as moderator. The section on rheumatism has scheduled a panel discussion, "Therapy of the Arthritides," for Tuesday, 11:05 a. m. The section on obstetrics and gynecology will hold a joint meeting with the committee on maternal welfare Tuesday afternoon, at which a panel discussion, "Lessons from Maternal Deaths—Obstetrical Emergencies," will be presented. The section on dermatology will close with "Treatment of Cancer of the Skin" by Dr. Richard L. Sutton Jr., Kansas City, Kan. A symposium on proteinuria will be held at the section on general practice Wednesday morning. The section on neuro-

psychiatry has scheduled its symposium, "Progress in Neurosurgery, Neurology, and Psychiatry," for Wednesday morning. The woman's auxiliary will meet concurrently.

NEW YORK

Transfusion Accidents.—At a meeting May 15 in the MacNaughton Auditorium, Brooklyn, the Medical Society of the County of Kings will present "Transfusion Accidents—Prevention and Treatment" by Dr. J. Edward Hall, associate professor of obstetrics and gynecology, and Dr. Louis M. Hellman, professor of obstetrics and gynecology, State University of New York College of Medicine at New York City, Brooklyn. Discussion and summary will be given by Dr. Alexander S. Wiener, attending immunohematologist, Jewish and Adelphi hospitals, Brooklyn.

New York City

Society News.—The New York chapter, International Academy of Proctology, will hold its annual meeting May 14, 8:30 p. m., at the Hotel Plaza, Fifth Avenue and 59th Street. Discussion from the floor will follow consideration of "Management of the Complicated Anal Fistula" by Dr. Edward Levy of Fordham Hospital. Members of the medical profession are cordially invited to attend.

Clinical Conference on Cardiology.—At its quarterly clinical conference May 15, 8:30 p. m., St. Clare's Hospital (426 W. 52nd St.) will present a panel, "Coronary Thrombosis," moderated by Dr. William B. Rawls, attending physician, New York Polyclinic Medical School and Hospital. The panel members will be Drs. J. Scott Butterworth, attending physician, Bellevue and University hospitals; Charles A. R. Connor, associate cardiologist, Lenox Hill Hospital; and Robert A. O'Connor, associate cardiologist, St. Clare's Hospital.

PENNSYLVANIA

Program on Arteriosclerosis.—The Allegheny County Medical Society will hold its annual scientific session and dinner at the Hotel William Penn, Pittsburgh, May 16. The meeting is open to the medical profession. From 2:30 to 4:30 p. m. Dr. Thomas Parran, dean, graduate school of public health, University of Pittsburgh, will serve as moderator for the following program on "Arteriosclerosis—A Challenge in Prevention and Management:"

- Complications of Treated Hypertensive Disease, Arthur C. Corcoran, assistant director, research division, Cleveland Clinic.
- Possible Accessory Factors in the Causation of Atherosclerosis, Henry A. Schroeder, associate professor of medicine, Washington University School of Medicine, St. Louis.
- Arteriosclerosis and Personality Change, Frederic L. Weniger, clinical director, Western Psychiatric Institute and Clinic, Pittsburgh.
- Physical Restoration of the Arteriosclerotic, Murray B. Ferderber, assistant professor of medicine, University of Pittsburgh.

At the annual dinner, 7 p. m., Mr. Arthur Treacher will have as his theme "A Little of This, Something of That, Mostly Humor." Interns, residents, and ladies are invited.

Meeting on General Practice.—The Pennsylvania Academy of General Practice will hold its eighth annual convention at the Bedford Springs Hotel, Bedford, May 18-20. The scientific program on Saturday will include the following speakers:

- Edward A. Marshall, director of medicine, Huron Road Hospital, Cleveland, Treatment of Peptic Ulcer—Unrestricted Diet.
- William D. Stroud, chairman, department of cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Coronary Artery Disorders.
- Benjamin Manchester, assistant clinical professor of medicine, George Washington University School of Medicine, Washington, D. C., Management of Anticoagulant Therapy.
- George T. Pack, attending surgeon, Pack Medical Group and Memorial Center for Cancer and Allied Diseases, New York City, Surgical Management of Primary and Metastatic Tumors of the Liver.
- Newlin F. Paxson, chief, division of women, Hahnemann Medical College and Hospital, Philadelphia, Induction of Labor, Its Use and Abuse.
- Leandro M. Tocantins, professor of clinical and experimental medicine, Jefferson Hospital, Philadelphia, Endocrine Therapy of Disorders of the Blood.

Nonmembers are welcome. There will be a banquet and dance Saturday.

Society News.—The Pennsylvania Academy of Physical Medicine and Rehabilitation will meet at 9 p. m. May 17 in the Philadelphia County Medical Society Building, 21st and Spruce streets. Dr. Samuel J. Prigal, department of allergy, New York Medical College and Flower and Fifth Avenue Hospitals, New York, will discuss "Aerosol Therapy." All physicians, interns, and physical therapists are cordially invited to attend.

SOUTH CAROLINA

State Medical Meeting at Myrtle Beach.—The South Carolina Medical Association will hold its 108th annual session May 15-17 at the Ocean Forest Hotel, Myrtle Beach, under the presidency of Dr. Orlando B. Mayer, Columbia. Scientific films will be shown Wednesday morning. The scientific session will open at 3 p. m. Wednesday afternoon with "The Medical Aspects of Cerebral Palsy" by Dr. Meyer A. Perlstein, Chicago, after which Dr. Denton A. Cooley, Houston, Texas, will discuss "Treatment of Aneurysm and Occlusive Diseases of the Aorta." Thursday at 9:45 a. m. "The Clinical Importance of Human Blood Groups" will be presented by Dr. Louis K. Diamond, Boston. At 10:15 a. m. Dr. C. Hampton Mauzy, Winston-Salem, N. C., will have as his subject "The Induction of Labor." A panel, "The Uses and Abuses of ACTH and Cortisone," will be presented at 4:30 p. m. Wednesday afternoon; a panel, "The Newer Aspects of Blood Dyscrasias," Thursday at 11:15 a. m.; and a panel, "Peripheral Vascular Disease," at 2:15 p. m. A clinicopathologic-therapeutic conference is scheduled for 4 p. m. Thursday. In addition to the essayists already mentioned, out-of-state speakers who will participate in the program include: Drs. William S. Howland and William T. Foley, New York; Dr. David F. James, Atlanta, Ga.; Dr. Claude Starr Wright, Augusta, Ga.; and Dr. C. Stuart Welch, Albany, N. Y.

VERMONT

Clinical Meeting.—The May Clinical meeting will be held May 17, 9:15 a. m.-4:00 p. m. at the Ethan Allen Club, 298 College St., Burlington, under the sponsorship of the Vermont State Medical Society; Vermont chapter, American Academy of General Practice; University of Vermont College of Medicine, Burlington; and the Vermont Heart Association. The morning program will conclude with a panel on rheumatic diseases, 10:45 a. m.-12 noon, with Dr. Robert E. O'Brien, Winooski, as moderator. The afternoon session will end with a panel on coronary artery disease, 2:45-4:00 p. m., moderated by Dr. Borys Surawicz, Burlington.

WEST VIRGINIA

Meeting on Allergy.—The regional meeting of the West Virginia chapter of the American Academy of General Practice at the Chancellor Hotel in Parkersburg, May 20, will be devoted exclusively to a discussion of allergy. Drs. Leo H. Criep and Jack D. Myers, of the department of medicine and allergy section of the University of Pittsburgh School of Medicine, will be the lecturers. Topics for discussion will be: Allergic Diagnosis; Allergic Management—Specific; Pediatric Allergy; Nasal Allergy; Skin Allergy; Bronchial Asthma; Chronic Vascular Headache; and Differential Diagnosis and Treatment of Cardiac Asthma. The first session will begin at 9:30 a. m. and the second at 1 p. m.

WISCONSIN

Society News.—The Madison Art Association is sponsoring an art show at the Wisconsin Neurological Foundation, 1954 E. Washington Ave., Madison, May 6-26, in which the paintings of John Bergman of Sheboygan will be exhibited. Many of his works have been completed since October of last year, during which time Mr. Bergman has been hospitalized at the foundation. The Wisconsin Painters and Sculptors Exhibitions at the Milwaukee Art Institute have included work by Bergman each year since 1949. The permanent collection in the Memorial Union at the University of Wisconsin includes one of his paintings and a piece of sculpture, and he has a painting in the permanent collection at the Milwaukee Art Institute. During the International College Students Traveling Exhibition in 1949, some of his work was exhibited in the National Gallery of Modern Art in Rome, Italy.

GENERAL

Clinical Workshops in Cardiology.—The American College of Cardiology has inaugurated a clinical workshop program, which is available free to all members of the medical profession. It will furnish person-to-person contact in the office, clinic, hospital, and laboratory with outstanding pioneers in scientific and clinical cardiology. Workshop centers have been made available in North and South America, Canada, Argentina, and Mexico. Application blanks may be obtained from Dr. Joseph B. Wolffe, Chairman, Clinical Workshop Committee, Valley Forge Heart Institute and Hospital, Fairview Village, Pa.

Meeting on Nuclear Technology.—An Industrial Nuclear Technology Conference covering the nonpower aspects of nuclear technology will be cosponsored May 15-16 by the Armour Research Foundation of the Illinois Institute of Technology and *Nucleonics Magazine* at the Museum of Science and Industry, 57th Street and South Shore Drive, Chicago. The session Wednesday morning will be devoted to biological applications, with Dr. George V. LeRoy, professor of medicine and associate dean, division of biological sciences, University of Chicago, as chairman. The concluding paper of this session, "The Next Five Years," will be presented by Dr. John C. Bugher, Washington, D. C., former director, division of biology and medicine, Atomic Energy Commission, and director, medical education and public health, Rockefeller Foundation, New York.

Symposium on Research Methods.—A Symposium on Recent Developments in Research Methods and Instrumentation will be held in conjunction with the sixth annual research equipment exhibit May 14-16 at the Clinical Center Auditorium, National Institutes of Health, Bethesda, Md., under the sponsorship of the Washington sections of the American Chemical Society, Society of American Bacteriologists, American Association of Clinical Chemists, Society for Experimental Biology and Medicine, and the Instrument Society of America. Topics will include: (1) Protein Structure by Physical Methods, (2) Advances in Methods of Emission Spectroscopy: Optical, X-Ray, and Gamma Ray Spectra, (3) Vapor-Phase Chromatography, (4) Low-Level Radioactive Counting Methods, and (5) Physicochemical Methods for the Study of Individual Living Cells. The scientific public is invited to attend the exhibit and the symposium.

Positions Open in Canal Zone.—The Health Bureau in the Canal Zone expects to have vacancies in ophthalmology, pediatrics, and pathology in the near future. The positions entail full-time practice at Gorgas Hospital in Ancon, which is approved for internship training and for residency training in ophthalmology, pediatrics, pathology, and other specialties. Applicants are required to be diplomates in their respective specialties or to be board eligible. Starting salaries range from $10,806.25 to $12,581.25, according to training, experience, and type of position. Free transportation to the Canal Zone is provided for the appointee, his legal dependents, and household goods. Family housing is available. There are schools and churches under standard American living conditions. About 8 weeks' leave, credited annually, may be accumulated to a total of 18 weeks. For information write to: Personnel Director, Balboa Heights, Canal Zone.

Society News.—A scientific meeting of the **American Otorhinologic Society for Plastic Surgery** will be held at the Waldorf-Astoria Hotel, New York City, May 18. An operative clinic the following morning at the Montefiore Hospital will consist of medicodental presentations and plastic surgery of the head and neck.——Officers of the **Congress of Neurological Surgeons** include Dr. Bland W. Cannon, Memphis, Tenn., president, and Dr. Frederick C. Rehfeldt, Fort Worth, Texas, vice-president. ——Officers of the **American Academy of Forensic Sciences** include Dr. Alan R. Moritz, Cleveland, president; Dr. Val B. Satterfield, St. Louis, president-elect; and Dr. Walter J. R. Camp, Chicago, secretary-treasurer.——Newly elected officers of the **Western Society of Electroencephalography** include Dr. Arthur A. Ward Jr., Seattle, president; Donald B. Lindsley, Ph.D., Los Angeles, vice-president; and Dr. Sylvester N. Berens, Seattle, secretary-treasurer.

Meeting on College Health.—The 34th annual meeting of the American College Health Association will convene May 17-19 at the Nicollet Hotel, Minneapolis, where the host will be the North Central Section. Dr. John W. Brown, University of California, Berkeley, will deliver the president's address Thursday, 10:30 a. m., and will preside at the association banquet that evening, at which the speaker will be Malcolm M. Willey, Ph.D., vice-president, academic administration, University of Minnesota, Minneapolis. Dr. Brown will also preside at the association luncheon Friday, when Dr. Joseph B. Wheelwright, University of California, San Francisco, will discuss "Public Relations and the Student Health Service." Thursday afternoon Dr. Jay A. Myers, University of Minnesota Medical School, Minneapolis, will have as his subject "Thirty-Five Years of Experience in the Chest Clinic of a Students' Health Service." At 3:30 p. m. there will be tours of the Mayo Memorial Building and Students' Health Service.

Exhibit of Medicine in Ancient Peruvian Art.—Physicians and others attending the annual meeting of the American Medical Association in Chicago June 11-15 will have an opportunity to see an exhibit of Medicine in Ancient Peruvian Art at the Chicago Art Institute on Michigan Avenue at Adams Street. Chicago is said to have the greatest collection of ancient Peruvian art in the world, and a great part of this ancient art, especially in ceramics, concerns medicine. The exhibit, arranged by Alan R. Sawyer of the Art Institute of Chicago and Dr. Leon Goldman, professor of dermatology at the University of Cincinnati College of Medicine, will comprise about 30 ancient Mochican ceramics, which represent various diseases, glandular disturbances, and physical deformities current around the beginning of the Christian era, surgical instruments used in such pre-Columbian operations as trepanning, and mace heads of the type that caused the wounds that made trepanning necessary. These objects come from two collections at the Art Institute of Chicago: the Dr. Eduard Gaffron collection, which the institute recently purchased, and the Nathan Cummings collection, formerly the B. J. Wasserman collection of Buenos Aires, Argentina.

Annual Cardiology Meeting in Chicago.—The American College of Cardiology will hold its fifth annual convention at the Drake Hotel, Chicago, May 16-19, under the presidency of Dr. Walter S. Priest, Chicago. Dr. Simon Dack, president-elect, will be installed as president on Wednesday. The opening address, "Experimental Heart Failure," will be delivered Wednesday at 3:45 p. m. by Dr. William F. Hamilton, Augusta, Ga. The Franz Groedel Lecture, "Medicine and Humanities," by Dr. John F. Fulton, New Haven, Conn., is scheduled for Wednesday, 8:30 p. m. Dr. Charles W. Crumpton, Madison, Wis., will serve as moderator for a symposium on chronic cor pulmonale Thursday morning. Thursday afternoon a symposium on catheterization and angiocardiography will be moderated by Dr. Francis F. Rosenbaum, Milwaukee, and a symposium on heart failure Friday morning will have as moderator Dr. Chauncey C. Maher, Chicago. The scientific sessions will close Friday afternoon with a symposium on therapy, for which the moderator will be Dr. Leo Loewe, Brooklyn, N. Y. Panel discussion will follow each symposium. Eight fireside conferences are scheduled for Friday evening, 8-10 p. m., with Drs. Clayton J. Lundy and Jacques M. Smith, Chicago, as moderators. The annual reception and banquet will be held Thursday evening, 6:30 p. m.

Postgraduate Courses Not Previously Published.—Notification of the following courses has recently been received:

A course in **histopathology of the eye** will be given by Dr. Gerald B. Kara, ophthalmic pathologist to the State University of New York College of Medicine at New York City, June 4-9. For details, contact Mrs. Jackson, IN 2-4000, Ext. 343 or write c/o Department of Ophthalmology, State University of New York College of Medicine at New York City, 451 Clarkson Ave., Brooklyn 3.

A postgraduate medical series of special courses for the summer of 1956 has been announced for the University of California Medical Center in Los Angeles by the University of California at Los Angeles School of Medicine and University Extension. The summer series is open only to graduates of approved medical schools with the consent of the course chairmen. In addition, two seminars on **hypnosis** are also available to graduates of approved dental schools and psychologists with Ph.D. degrees. Courses planned, together with dates and hours of meetings, are: Recent

Advances in **General Surgery,** July 16-18, 9 a.m.-12:30 p.m. and 2-5 p.m.; **Surgery of Trauma,** July 19-20, 9 a.m.-12 noon and 2-5 p.m.; Recent Advances in Medicine: Current Topics in **Internal Medicine,** July 23-27, 9 a.m.-12:30 p.m. and 2-5:30 p.m.; and **Anesthesia:** Problems in Selection, Aug. 27-29, 9 a.m.-12 noon and 2-5 p.m. Information or detailed programs on any of these courses are available by addressing Dr. Thomas H. Sternberg, Assistant Dean for Postgraduate Medical Education, University of California Medical Center, Los Angeles 24.

The postgraduate department of the University of Tennessee College of Medicine, Memphis, will offer a program in **cardiovascular diseases** May 23-25 under the direction of Dr. I. Frank Tullis, chief of the division of medicine, and one in abdominal surgery July 25-27 under the direction of Dr. Harwell Wilson, chief of the division of surgery. The fee for each course is $50.

Geriatrics Meeting.—The National Social Welfare Assembly announces a meeting of the National Committee on the Aging at the Sheraton-Lincoln Hotel, Indianapolis, May 17-19, in cooperation with the Indiana State Commission on the Aging and Aged and the committee on aging of the Health and Welfare Council of Indianapolis and Marion County. The theme, "Maintaining Independence in Old Age," will be introduced Thursday, 4-6 p. m., through four films: "A Place to Live" (standards of care in homes for the aged); "Still Going Places" (rehabilitation of the aged); "Our Senior Citizens" (a day-center program for older people); and "Home Care" (extension into the home of hospital care for the chronically ill). "Independence Through Good Health" will be the theme of the dinner meeting ($3.30), 6:30-9:45 p. m., at which "Current Approaches to Health in Old Age" will be discussed by Dr. Bertram Groesbeck Jr., Indianapolis, director, Indiana State Department of Health, and "Health Maintenance Programs in Industry" by Dr. Emmett B. Lamb, Indianapolis, medical consultant, International Harvester Company and P. R. Mallory Company. During the Friday morning program on "Achieving Independence Through Peace of Mind," "The Psychiatrist Sees the Older Person" will be presented by Dr. Jack Weinberg, Michael Reese Hospital, Chicago, and "Use of Tranquilizing Drugs" by Dr. Bill L. Martz, director, Lilly Clinic, Indianapolis General Hospital. A panel and general discussion on preparation for retirement will be held Friday afternoon and a workshop on community organization Saturday morning.

CANADA

Meeting of American Laryngological Association.—The 77th annual meeting of the American Laryngological Association will be held May 13-14 at the Seigniory Club, P. Q., Canada, under the presidency of Dr. Bernard J. McMahon, Clayton, Mo. The guest speakers will be Frank C. MacIntosh, Ph.D., McGill University, Montreal, who will consider "Histamine Releasing Drugs" Sunday morning, and Dr. Fernand L. Montreuil, Montreal, who will present "Carcinoma of the Larynx" Monday morning. The guest of honor will be Dr. George M. Coates, Philadelphia.

Meeting on Otorhinolaryngology.—The 60th annual meeting of the American Laryngological, Rhinological and Otological Society will convene at the Sheraton-Mt. Royal Hotel, Montreal, May 15-17. After a welcome by Dr. G. Lyman Duff, dean of medicine, McGill University Faculty of Medicine, Montreal, Tuesday, presidential remarks will be delivered at 9:30 a. m. by Dean M. Lierle, Iowa City, and the guest of honor, Dr. Harold I. Lillie, Rochester, Minn., will be introduced. The scientific session will open with "Evolution of Surgical Technique in the Treatment of Carcinoma of the Larynx" by Drs. Chevalier L. Jackson and Charles M. Norris, Philadelphia. At 10:45 a. m. Dr. Howard A. Rusk, New York, will speak on "Sick People in a Troubled World." At 12:05 p. m. "Observations on Plasma Proteins in Relation to Allergy" will be presented by Dr. Bram Rose, Montreal. On Wednesday, 10:05 a. m., a motion picture, "One State Repair of Hypopharyngeal Diverticulum" will be shown by invitation by Dr. Edgar S. Brintnall, Iowa City, after which "Theory and Practice of Tympanoplasty" will be discussed by Prof. H. Wullstein, Wurzburg, Germany. At 11:15 a. m. a motion picture, "Automobile Fractures of the Larynx," will be shown (authors, Drs. Paul H. Holinger and Kenneth C. Johnston, Chicago; co-authors, Drs. Paul W. Greeley, Chicago, and John W. Curtin, Chicago). Dr. John M. Converse, New York, will discuss "Corrective Surgery of the Nasal Tip" at 11:05 a. m., preceding the International Broncho-Esophagological luncheon at 12:30 p. m. The Thursday session will open with "Surgical Treatment of Carcinoma of the Anterior Commissure of the Larynx" by Drs. F. Johnson Putney and Enrique A. Vicens, Philadelphia. At 11 a. m. Thursday a symposium will be presented on "The Operation for the Mobilization of the Stapes in Otosclerotic Deafness." The profession is cordially invited to attend. The social program includes a civic reception at the Chalet on top of Mount Royal Tuesday evening, which will be given by Mayor Jean Drapeau of Montreal, and a banquet Wednesday, 7 p. m., preceded by cocktails at 6 p. m.

LATIN AMERICA

Pan American Congress of Gerontology.—The first Pan American Gerontological Congress will meet in University City of Mexico, Sept. 15-22, instead of Sept. 7-15 as previously announced (THE JOURNAL, Jan. 21, page 220). The registration fee will be $10. Subjects for discussion will include: Psychologic Problems of Retirement; Sociologic Studies of Old Age; Legislation for the Aged; Social Rehabilitation; and Psychology and Correlated Problems of Very Old Men. Information may be obtained from Dr. Manuel Payno, Avenue Cuahtemoc No. 10-3, Mexico 7, D. F., Mexico, president, or from Dr. Edmund V. Cowdry, Washington University School of Medicine, St. Louis 10, who is chairman of the North American committee of cooperation for the congress.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations in the United States and Canada, July 20. Final date for filing application was Jan. 20. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY. *Written.* Various centers, July 26. *Oral.* St. Louis, Oct. 12-15. Final date for filing applications was April 1. Sec., Dr. B. M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 15, 1956. Final date for filing application is May 1. *Oral Examinations in 1956.* Chicago, June 7-9. Final date for filing application for these three oral examinations was Jan. 3. New York City, Sept. 21-25. Final date for filing application was April 1. *Cardiovascular Disease.* Chicago, June 6. The number of candidates is limited to 24 and the final date for filing applications was Apr. 2. Exec. Sec., Dr. William A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral and Pathological Examinations. Part II.* Chicago, May 11-20, 1956. *Part I.* Applications now being accepted. Final date for filing applications is Oct. 1. Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical Examination.* San Francisco, June 18-21, St. Louis, Oct. 20-24. *Written.* Jan. 21, 1957. Applications must be filed before July 1, 1956. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral. Part II.* Chicago, January 1957. Final date for filing application is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF PEDIATRICS: *Oral, Part II.* Cincinnati, June 8-10; New York City, Oct. 12-14, and San Francisco, Dec. 7-9. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Parts I and II.* Chicago, June 16-17. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY. *Entire Examination.* Buffalo, May 13-15. Final date for filing case reports was Jan. 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF RADIOLOGY: Chicago, June 5-9. Final date for filing applications was Jan. 1.; Los Angeles, Sept. 30-Oct. 4. Final date for filing applications is June 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Boston, May 14-15 and Philadelphia, June 4-5. Sec., Dr. John B. Flick, 255 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: February 1957. Sec., Dr. William Niles Wishard, 1711 N. Capitol Ave., Indianapolis 7.

BOARD OF THORACIC SURGERY. *Written.* Various centers throughout the country, September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

DEATHS

Scott, Arthur Carroll, Jr. ✠ Temple, Texas; born in Gainesville Dec. 19, 1890; Harvard Medical School, Boston, 1918; interned at the Massachusetts General Hospital in Boston; entered the Mayo Foundation at Rochester, Minn., and left April 1, 1920; member of the House of Delegates of the American Medical Association from 1949 to 1955, chairman of the special committee on general practice, prior to specialization, and member of the Council on Medical Service; member of the Southern Surgical Association; fellow of the American College of Surgeons, member of the founders group of the American Board of Surgery; at one time chairman of the city health commission; served as chief surgeon at the Gulf, Colorado and Santa Fe Hospital, and as president of the Scott and White Clinic; died in Lubbock Feb. 21, aged 65.

Allen, Wilson Pruitt ✠ Woodbury, Ga.; Atlanta College of Physicians and Surgeons, 1907; died Feb. 29, aged 72.

Apfel, M. Marion, New York City; University of the City of New York Medical Department, New York City, 1893; served on the staff of Unity Hospital in Brooklyn; died March 4, aged 82, of cancer.

Berge, Fritjof Emil, Manhattan Beach, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1894; an associate member of the American Medical Association; served on the staff of the California Hospital; died in the Torrance (Calif.) Hospital Jan. 11, aged 87, of pulmonary edema and coronary heart disease.

Cleveland, Ernest Schuyler, Colfax, Ind.; Chicago College of Medicine and Surgery, 1913; for many years a member of the staff of the Norwegian American Hospital; medical director for Carson Pirie Scott & Company in Chicago for 41 years, retiring in 1951; died March 9, aged 70, of tuberculosis.

Doremus, Widmer Elijah, Winter Park, Fla.; New York Homeopathic Medical College and Hospital, New York City, 1901; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; served during World War I; died Feb. 14, aged 77, of myocardial infarction.

Griffin, Guy Bray ✠ Orange, N. J.; Tufts College Medical School, Boston, 1930; certified by the National Board of Medical Examiners; fellow of the International College of Surgeons and the American College of Surgeons; interned at St. Vincent's Hospital of the City of New York; senior surgeon at St. Mary's Hospital; died in the University of Pennsylvania Graduate Hospital in Philadelphia Feb. 10, aged 58, of hepatitis.

Hamlin, Frederick J., Peoria, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1901; aged 80; was suffocated Feb. 21 in his smoke-filled apartment, after the building caught fire, apparently from an overheated coal stove.

Lasater, James Harvey, Sr., La Center, Wash.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1905; served on the staff of the Vancouver (Wash.) General Hospital; died Feb. 3, aged 78.

Legge, Kenneth Dartmouth, Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; professor of clinical urology at his alma mater; an associate member of the American Medical Association; member of the American Urological Association; died in St. Mary's Hospital in West Palm Beach, Fla., Jan. 22, aged 60, of coronary occlusion.

Monahan, Thomas Aloysius, Shenandoah, Pa.; Jefferson Medical College of Philadelphia, 1905; past-president of the school board; served during World War I; for many years on the staff of the Danville (Pa.) State Hospital; died in the Locust Mountain State Hospital March 1, aged 76, of cerebral thrombosis.

✠ Indicates Member of the American Medical Association.

Ortschild, John Francis, Beaverton, Ore.; Johns Hopkins University School of Medicine, Baltimore, 1906; died in Hillsboro Jan. 26, probably of a recurrent cerebral vascular accident.

Patterson, Charles Fuller, Pacific Palisades, Calif.; Fort Wayne College of Medicine, 1898; died Jan. 25, aged 87.

Peterson, Albert Alonzo, Pasadena, Calif.; Jefferson Medical College of Philadelphia, 1901; an associate member of the American Medical Association; died Jan. 15, aged 78, of acute pulmonary edema.

Pettiford, William Bryant, Raleigh, N. C.; Meharry Medical College, Nashville, Tenn., 1929; medical director at Shaw University; on the staff of St. Agnes Hospital, where he died Jan. 26, aged 61, of carcinoma of the prostate.

Plane, John Fredrick ✠ Corvallis, Ore.; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1903; member of the California Medical Association; for many years practiced in Long Beach, Calif., where he served as chief of the staff at the Community Hospital; died Jan. 7, aged 80, of pulmonary fibrosis and carcinoma of the prostate.

Price, Earl Sanders ✠ Tuscaloosa, Ala.; Emory University (Ga.) School of Medicine, 1916; served during World War I; staff member at Druid City Hospital, where he died Jan. 27, aged 71, of injuries received in an automobile accident.

Robinson, John Fletcher, Mount Vernon, Ohio; Albany (N. Y.) Medical College, 1906; at one time on the staff of the Mayo Clinic in Rochester, Minn.; fellow of the American College of Surgeons; served on the staff of the Mount Vernon State Hospital; died in England Nov. 27, aged 73.

Sands, Herman Charles, Salem, Mass.; Middlesex University School of Medicine, Waltham, 1942; member of the Massachusetts Medical Society and the American Academy of General Practice; served during World War II; on the staff of the Josiah B. Thomas Hospital in Peabody; died in the Baker Memorial Hospital in Boston Dec. 6, aged 39, of Hodgkin's disease.

Sartori, Henry J., San Francisco; Cooper Medical College, San Francisco, 1893; an associate member of the American Medical Association; on the staff of St. Joseph Hospital and St. Francis Memorial Hospital; medical examiner for the Mutual Benefit Life Insurance Company; died Feb. 7, aged 84, of carcinoma.

Schugt, Henry Paul, New York City; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; consultant at St. Francis Hospital in Port Jervis, N. Y.; on the staff of the Lenox Hill Hospital, where he died Jan. 30, aged 60, of cerebral hemorrhage.

Taylor, Ralph Leland ✠ Davisboro, Ga.; University of Maryland School of Medicine, Baltimore, 1911; served as a member of the school board of Davisboro; for 20 years chairman of the county school board; died in the Georgia Baptist Hospital, Atlanta, Jan. 22, aged 68, of uremia.

Washburn, Will Warren ✠ Lafayette, Ind.; Indiana University School of Medicine, Indianapolis, 1925; past-president of the Tippecanoe County Medical Society; specialist certified by the American Board of Urology; member of the American Urological Association and Aero Medical Association; served during World War II; on the staff of the Lafayette Home Hospital and St. Elizabeth Hospital, where he died Feb. 10, aged 55, of cancer.

Zweig, Ludwig ✠ Olean, N. Y.; Rheinische Friedrich-Wilhelms Universität Medizinische Fakultät, Bonn, Prussia, Germany, 1909; served as resident at the Brigham Hall Hospital in Canandaigua; consultant on the staff of St. Francis Hospital; honorary member of the staff of the Olean (N. Y.) General Hospital; died in Los Angeles Dec. 13, aged 72, of hypertension and cerebral thrombosis.

FOREIGN LETTERS

AUSTRIA

Social Security Law.—The fact that insured wage earners were to be treated in the same way as salaried employees was regarded as a special advantage of the new general social security law (ASVG). It was to give workers the right to go to contract physicians for roentgenologic examinations and for physical therapy, rather than insisting that they use the facilities of the health insurance companies, as was the case before the law was enacted. The workers who had looked forward to being able to choose their own physician have, however, been disappointed again. Although the new law insures the right of free choice of physician, Circular Letter no. 72, Dec. 27, 1955, of the health insurance district of Vienna overrules this change and states that the contracts entered into with physicians remain in force until new contracts have been made in accordance with the regulations of the new law. Exceptions are the regulations on the dissolution of the contractual relationship and on the arbitration of disputes. Thus, there will be, for the time being, no change as regards the type and extent of the services rendered by insurance physicians, as well as regarding fees for contract physicians. Likewise, the regulation that those insured with the main office of the health insurance district of Vienna are not permitted to consult contract physicians for roentgenologic examination and physical therapy will remain in force. For consultation with a physician of their own choice, the health insurance companies will repay to the insured the costs according to set tariffs. If, however, a contract physician engages in private practice or if the insured, in the same insurance case, consults in addition to the physician of his choice a contract physician, a health insurance clinic, or a contract institute, then the costs for the self-selected physician will not be repaid. Through this regulation the insurance companies again completely disregard the expressed purpose of the law.

Surgical Treatment of Glioblastoma.—At the meeting of the Society of Physicians in Vienna on March 2, Dr. D. Krüger stated that malignant glioblastomas are the commonest of the true cerebral tumors, accounting for about 30% of the total. Preoperative diagnosis of the type is important; it may be made with the aid of serial angiography in 60% of the cases. The prognosis is poor, as most of these patients die within a year of the onset. Little improvement can be obtained with roentgen irradiation. The condition of a patient who lives two years after surgical removal of the tumor must have been erroneously diagnosed; the tumor probably was an oligodendroglioma. Exploratory trephining may be required from time to time. Treatment with cobalt-60 seems to be promising. In about 80 patients treated by this method, Klar observed a surprisingly long survival time. This method should therefore be used on a larger scale.

Direct Cholangiography.—At the same meeting, Dr. F. Mandl reported that failure of intravenous cholangiography with iodipamide sodium in patients with jaundice has advanced a direct method in which a 50% solution of morpholine salt of diiodized pyridone (Ioduron) is introduced through the skin into a bile duct. This was done successfully without causing any damage in 15 or 25 patients. No operation should be performed immediately after the cholangiography. Cholangitis is also a contraindication. Roentgenograms thus obtained clearly revealed the differences in the appearance of isolated stones in the common bile duct, carcinoma of the pancreas, bile duct sludge, hepatitis, and metastases of the liver, often after the usual laboratory examinations had failed to indicate the diagnosis.

Society for History of Medicine.—Prior to 1938, the Society for History of Medicine in Vienna was the largest society of its kind in the world. Prof. M. Neuburger, who then held the chair of medical history in the University of Vienna, had on his own initiative established the world's second largest medical history institute. When Professor Neuburger left Vienna for political reasons in 1939, the society became defunct. After his death last year, a group of his former students and friends instigated a movement to reactivate the society, and in January, 52 Austrian physicians and surgeons met for this purpose. A major object of this society will be to restore, enhance, and enlarge the present History of Medicine Museum of the University of Vienna. It is also proposed to publish a book entitled "Vienna's Contribution to World Medicine: Vienna, Cradle of Medical Specialties."

The items in these letters are contributed by regular correspondents in the various foreign countries.

BRAZIL

Mycotic and Trichomonal Vaginitis.—Dr. C. A. Ferreira reported in *Anais brasileiros de ginecologia* (**41**:65, 1956) that certain special aspects of the colpocytogram may help in the diagnosis of a few local inflammatory or parasitic processes. In patients with trichomonal vaginitis, the diagnosis can be made even before the finding of the causative agent and with low-power magnification through the presence of great numbers of pus cells and a high percentage of eosinophils. Even when there are few parasites, it is possible to see a fine, colored "dust" between the cells and even on them. These particles are smaller than cocci, are different from Hemophilus vaginalis, and give the impression of being formed by some substance produced by the metabolism of the Trichomonas. Stained by Schiff's stain, this material appears to contain polysaccharides. Stained smears of specimens from 744 patients showed the presence of Trichomonas organisms in 69 of them (9.3%). Of these, the smears from 53 disclosed the blurred aspect described, those of 60 showed an abundance of pus cells, those of 22 showed eosinophils, and those of 57 showed inflammatory changes. Cytologically, the condition found by colpogram was almost always normoestrogenic, being hypoestrogenic in only 10 cases and atrophic in 5. In the entire series, there were 27 patients with mycosis (3.8%), and, of these, pus cells were present in the smears of only 18. The normoestrogenic condition was found in 88.8% of the smears, the hypoestrogenic in 7.4%, and the atrophic in 3.7%. Cytolysis was found in 5.8% of these cases and cellular inflammatory changes in 51.8%. Eosinophilia was found in 33.3%.

Cancer of the Colon and Rectum.—Paulino and Rodrigues, in *Revista brasileira de cirurgia* (**31**:5, 1956), reported the results of the surgical treatment in 62 successive cases of cancer of the colon and rectum, 57 of which were primary. Thirty-seven of the patients were men and 25 were women; their ages varied between 23 and 85 (average 55) years. In patients with cancer in the ascending colon, the chief findings were palpable tumor, anemia, and dyspepsia; in those with cancer in the descending colon, they were obstruction and blood in the stools. Loss of weight was observed in both groups. The authors recommend resection of the colon with end-to-end anastomosis in patients with no obstruction. If intestinal obstruction is present, it is better to decompress the colon through colostomy and perform a colectomy three or four weeks later. Of 48 patients who had a colectomy, 21 were alive, with no signs of recurrence or metastasis. In this group, the time elapsed since the operation was over five years in four patients, over four years in three, over three years in two, over two years in four, and over one year in eight.

Aortic Aneurysm.—Dr. Candido de Oliveira and his co-workers in *O Hospital* (**49**:283, 1956) reported that in a series of 4,200 autopsies aortic aneurysms were found in 78 of the patients. Dissecting aneurysms were not included. Seventy of these patients were men; 62 aneurysms were of the thoracic aorta, 14 were of the abdominal aorta, and 2 involved both portions. In 29 patients, death was caused by rupture. In most of the others, death was caused by respiratory obstruction or cardiac failure.

FRANCE

Asthenia and Adrenal Cortical Function.—Gilbert-Dreyfus and his co-workers reported to the Medical Society of the Hospitals of Paris on 11 patients with a syndrome characterized by an asthenia resembling that seen in adrenal insufficiency and decreased urinary 11-hydroxycorticoids and 17-ketosteroids. Corticotropin in intravenous infusion leads to immediate and massive adrenal response with sharp increase in the corticoids, showing that neither Addison's disease nor a secondary Addisonian syndrome are concerned. The patients are usually depressed, anxious, and psychasthenic (many in this series were former inmates of concentration camps). This would seem to indicate that the origin of the disorder is in the central nervous system, that is, the syndrome represents an inhibition of the hypophysis and the adrenals controlled by the cerebral cortex and the hypothalamus.

Immunity to Tuberculosis.—M. Pestel, reporting to the same society, said that the mechanism of the protection conferred on the human body by introduction of living microbes of attenuated virulence is of particular interest in view of cases of progressive pulmonary tuberculosis that appear in patients previously given BCG vaccine. The protection conferred by BCG vaccine has been shown experimentally to be neither absolute nor of infinite duration. Also, there is no means of determining in a given patient what the validity of the protection is at a particular time. It follows that a program of BCG vaccination in no way allows relaxation of mass inspection measures for tuberculosis. No healthy person should be permitted to come in contact with a tuberculous patient whose sputum contains bacilli, regardless of whether the person has been vaccinated or not. Early isolation and energetic treatment remain the essential methods of prophylaxis against tuberculosis. Improvements in therapy of the disease have removed the immediacy of the necessity for an obligatory system of vaccination, especially in young children. Perhaps, in view of the rise in the age at which primary infection is apt to occur and the potent methods of treating primary infection, the system of vaccination should be based on the socioeconomic level, standard of living, and organic deficiency, if any, of each prospective subject. Such a program would have the advantage of adjustment to individual requirements. It would also materially lessen the expense to the government of a well-controlled vaccination program.

Neuroplegics for Myocardial Infarction.—P. Broustet and his co-workers (*Presse méd.* **63:**1761-1763 [Dec. 24] 1955) compared the effects of opium derivatives and those of the lytic cocktail in treatment of myocardial infarction and its sequelae and intractable angina pectoris. The "cocktail" consisted of meperidine, promethazine, and chlorpromazine and was usually injected intramuscularly, sometimes given intravenously, and occasionally administered orally. The authors concluded that it is the best calming agent available for the treatment of infarction and its sequelae. It is better tolerated than morphine in that it does not lose its effect over a period of time and does not cause digestive disturbances; it is just as effective in reducing pain; and it is superior in combating shock. The lytic cocktail does not hinder the association of other therapeutic measures such as anticoagulants, vasodilators, and mercurial diuretics. It has no effect on the processes involved in myocardial infarction, nor can we be assured that it will save a greater number of patients with this disorder, but it can relieve the period of pain and shock better than the methods hitherto used.

Tuberculosis and Electroconvulsion.—Porot and Cohen-Tenoudji (*Presse méd.* **63:**1871-1874 [Dec. 31] 1955) state that tuberculosis is no longer one of the absolute contraindications to psychiatric shock treatment. In fact, electroshock is the best tolerated and most effective therapy for the agitation and insomnia that have such an adverse effect on the patient with tuberculosis. It must be reinforced by collapse or antibiotic therapy, even when the tuberculous process is to all appearances quiescent. The risk of reactivation or exacerbation is often less than that connected with nonintervention on the psychic symptoms. Insulin shock therapy is more dangerous and its indications are limited, but small doses have given good results and merit further trial, as does shock with acetylcholine. Pentylenetetrazol (Cardiazol) shock therapy should not be given to any patient with tuberculosis.

ITALY

Phenylbutazone.—At the meeting of the Italian Society of Gastroenterology in November, Professors Bellomo and Fusco reported on 10 normal or hypochlorhydric patients without organic lesions who were given phenylbutazone orally on an empty stomach. Samples of gastric juice were obtained for estimations of the free and total acidity and of the percentage of total gastric mucin and albumin. The speakers found that gastric secretion, after the administration of phenylbutazone, increased in eight of the subjects; the total quantity of juice secreted after the administration of the medicine was larger than the total quantity present in the fasting stomach. The acidity was higher in seven subjects after taking the drug than it had been during fasting. However, in two subjects who showed no change in the quantity of secretion, the acidity of the gastric juice was increased. One subject who while fasting had only traces of acid in the stomach showed an increase in both free and total acidity. In four subjects who had relatively small amounts of mucin and albumin while fasting, these components increased, especially the albumin, after phenylbutazone was given. Another group of five subjects who showed a high percentage of mucin while fasting had smaller amounts after the drug was given. In this group, the percentage of albumin showed no consistent behavior. Of the five subjects with a very high percentage of mucin while fasting, none showed blood in the gastric juice after the administration of phenylbutazone. The speakers concluded that the introduction of phenylbutazone by mouth acts as an immediate stimulus on the gastric mucosa, which is manifested with an increase in the quantity of juice secreted and an increase in acidity.

Endocrinological Meeting.—At the fifth National Congress of the Italian Endocrinological Society in Genoa in December, Silvestrini and Pasargiklian stated that palpebral edema, considered by some a pathognomonic sign of hyperthyroidism, does not always affect the two eyes equally or simultaneously. Disturbances in the motility of the eyes, though more frequent and severe in euthyroid patients with exophthalmos, may occur in patients with classical hyperthyroidism. The frequent finding of a high concentration of thyrotropin in the blood of patients with exophthalmos suggests an increase in hypophysial activity. The speakers believe that the roentgen irradiation of the hypothalamus and particularly of the hypophysis is the most effective and least dangerous method of therapy of the exophthalmos.

SWITZERLAND

Tuberculosis in Europe.—At a conference of Dutch and Danish health authorities in Copenhagen in March, 1955, it was brought out that for the period 1950-1953 the annual, average, reported incidence of tuberculosis was 51 cases per 100,000 population in Denmark and 123 per 100,000 in the Netherlands. This discrepancy was explained by the fact that in Denmark patients are counted and in the Netherlands cases are counted. In Holland, a relapse is considered a "new" case. In order to arrive at a better basis for comparing the tuberculosis rates between different countries, a World Health Organization study group on tuberculosis control met in Luxembourg in December. Representatives from Denmark, the Federal Republic of Germany, France, Italy, the Netherlands, Norway, Switzerland, and the United Kingdom participated. The group concluded that mortality figures are reasonably reliable and can be compared from country to country but bear little relation to the tuberculosis problem as a whole. The old rule that the number of beds required for tuberculous patients equals about twice the number of annual deaths from tuberculosis was found to be out of date. Although the case fatality rate for tuberculosis is declining, the number of cases of tuberculosis has not decreased very much. There is no evidence that eradication will be easy or that it will

become a practical possibility in the near future. The group strongly recommended that all cases of pulmonary tuberculosis be reported. Progress was also made in evaluating mass tuberculin testing, mass x-rays, and the compilation of national tuberculosis registers as means of measuring the tuberculosis problem. Some countries already have a central register, and the value of a properly kept register was clearly recognized by the group. For large countries, however, such a register is not practical. It is estimated that in Denmark the per capita cost of tuberculosis is $2 a year. In 1952, the Netherlands spent about 4 cents per capita on mass examinations for tuberculosis and about 9 cents on tuberculosis dispensaries. The cost of tuberculosis hospitals and sanatoriums, public assistance, disability pensions, and other costs must be added to this. In some countries with a low prevalence of tuberculosis, mass examinations revealed too few cases to be economically justifiable. Instead, efforts should be directed at special groups, particularly those exposed to infection and those likely to infect others, such as household contacts of tuberculous patients, hospital personnel, medical and dental students, schoolteachers, food handlers, older people (particularly men), hospital patients, seafarers, and, in some countries, students. For countries with a medium prevalence of tuberculosis, mass examinations will continue to be profitable for years to come. Efforts to control the infection in human beings should go hand in hand with a campaign to eradicate the infection in cattle, as there is a definite risk of the bovine type of the bacillus replacing the human type. Eradication of bovine tuberculosis has been achieved in Denmark. In the Netherlands it is nearly achieved, and in Great Britain great progress has been made. There is no evidence that the resistance of the tubercle bacillus to drugs will create a serious problem. One speaker even suggested that the spread of resistant strains of bacteria among the population might confer some immunity against the more serious forms of the disease. There is increasing interest in the complete rehabilitation of tuberculous patients.

UNITED KINGDOM

Poliomyelitis Vaccine Controversy.—The government's announcement that it proposed to rush through a spring program of poliomyelitis vaccination with a Salk-type vaccine has provoked much controversy because of (1) the precipitate and brusque manner in which the government announced the scheme without giving any warning or advanced information to the medical profession, (2) the resentment of certain local health authorities because they are to have no say as to which of the children in their areas are to be vaccinated, (3) the fear that the vaccine is not safe, and (4) doubt of the validity of this particular vaccination as a sound public health measure. The view of those who are worried about the long-term effect of the use of the Salk vaccine is summed up by Dr. W. R. Russell in a letter to *Lancet* (March 10, 1956, page 321) in which he points out that, to prevent three paralytic cases, 12,000 children must each be given two or more injections of the vaccine. This might be worthwhile if the protection lasted, but, unfortunately, it may persist for only a year or two. It is not known whether, after five years have elapsed, the partial protection will be maintained, lost, or even reversed. The long-term prospects for those now being given the Salk vaccine are so uncertain that the present American program may be described as a gigantic gamble.

Although many health officers have protested against the short notice they have been given, most of them have agreed to participate in the scheme. The health officer of Burton-on-Trent will not participate. Four years ago there was an outbreak of poliomyelitis in two areas in that town, and the local authority now wishes to concentrate the use of the vaccine in these two areas. This would not be permissible under the present scheme, because the decision as to which children in the selected age groups are to be vaccinated is made in London. For this reason, the health officer will not participate until sufficient vaccine is available to treat all the children whose parents will permit it. Sir Harold Himsworth, the secretary of the Medical Research Council, said that, if we may judge from the early experience in the United States, it is unlikely that the Salk vaccine will abolish poliomyelitis completely, although we may expect it to give a substantial measure of protection. It would be premature, therefore, to stop investigating alternative preventive measures, of which the most hopeful seems to be a vaccine made from living attenuated virus, which can be taken by mouth. Another field of research in which more work is needed is the elaboration of blood tests that the ordinary laboratory can use to guide the immunization policy and to provide a means of rapid diagnosis, especially of nonparalytic poliomyelitis, which at present is often difficult to distinguish from various other diseases.

Supplies of Gamma Globulin.—Gamma globulin, prepared from pooled plasma from healthy adults by the Lister Institute for the Ministry of Health, is distributed to physicians in England and Wales through laboratories of the Public Health Laboratory Service. The ministry has announced that so far as supplies allow, it will be issued for the protection of susceptible contacts of measles, rubella, and poliomyelitis in certain circumstances. In the case of measles, it is available for control of hospital and institutional outbreaks, for persons suffering from intercurrent illness or living in a poor environment and for whom an attack of measles would be dangerous, and for children under 3 years of age. In the case of rubella, the gamma globulin will be available for women exposed to infection in the first four months of pregnancy. In the case of poliomyelitis, it may be used for nurses and medical students who are to be closely associated with the care of early cases and who so far as is known have not been in contact with the infection previously (only one injection will be given and that prior to their going on the poliomyelitis wards), babies in a hospital exposed to infection soon after birth, and children in a hospital ward in which a case develops (especially children who have recently undergone tonsillectomy). In addition, a small stock of gamma globulin prepared from the blood of persons recently vaccinated against smallpox is held for the treatment of cases of generalized vaccinia and of accidental vaccinial infections endangering the eye and, in special circumstances, for the protection of unvaccinated smallpox contacts.

Experiment in Training Nurses.—An experimental course of training for student nurses is to begin in Glasgow Royal Infirmary in September. Formal study will be concentrated into a period of two years, instead of three as at present, the third year being devoted entirely to practical experience in the hospital. It will be the first course of its kind in the United Kingdom, and the aim is to provide training that will help to develop those qualities of leadership and judgment that are increasingly called for in holders of senior positions in the nursing profession. The course has been approved by the General Nursing Council for Scotland as qualifying for registration those who are successful in the examination. In the first two years there will be complete integration of theoretical and practical training to a much greater extent than has been found possible in a normal course of training. The students in this course will not be required to take the preliminary state examination, which has led to cramming in the early stage of the regular course. The students will take their final state examination at the end of two years but will not be eligible for registration until they have completed the third, or intern, year of hospital experience. In the third year, however, they will act in all respects as staff nurses.

Milk Tablets for Children.—The Education Act of 1944 required local authorities to give free milk to all children maintained in state schools, and until October, 1954, it was supplied and paid for by the Ministry of Food. Then the onus of ordering and payment was placed on the local education authorities. Owing to transport and weather difficulties, some schools have been unable to get fresh milk and the children have been given dried milk or milk tablets. Cost is an important consideration for some education authorities. The school milk bill for the country is about 28 million dollars yearly. The Minister of Education has given permission to six local authorities to issue milk tablets when the price of fresh milk has been unreasonable. Although there is no suggestion that milk tablets are as good as liquid milk, they are an adequate substitute. Fruit-flavored milk tablets have been produced and are liked by the children.

CORRESPONDENCE

THE AUTOPSY

To the Editor:—The guest editorial entitled "Potential Values of the Autopsy Today" (*J. A. M. A.* **160:**1144 [March 31] 1956) deserves an immediate reply for the defense of the autopsy system. Some may consider this to be a static procedure that should be eliminated from our educational program, but, as a pathologist, I am thoroughly convinced that the postmortem examination is not at the dead-end street, even though it does take place in the morgue. There is always a tremendous wealth of data to be culled from these autopsies, if they are carefully performed and supervised by an experienced and interested pathologist. If they prove to be a chore to some departments of pathology, this usually denotes the need of enlarging the staff. However, there are more fundamental reasons than this to account for the present predicament of pathology. Certainly the remedies suggested by the editorial would be ludicrous if they were not so serious to the future of our profession.

One of the principle reasons responsible for the attitude regarding pathology, in my opinion, has been the unusual and often unwise appointments to the chairs of pathology in some medical schools of today. A wide experience, intense interest in teaching, and a clear understanding of pathology in all of its aspects no longer qualifies one to head the department of pathology. Instead, an experimentalist, a physicist, or perhaps a clinician from a remotely related department is appointed to the full professorship of pathology. There are very few medical schools existing today in which there are men of the caliber of Welch, Karsner, Opie, MacCallum, Winternitz, Warthin, Oliver, and many others. These men were excellent gross pathologists and not afraid to impart their knowledge to the clinician at the autopsy table. Several of our recently appointed pathologists rarely enter the portals of the autopsy room and even refuse to perform an autopsy. It is more logical to assume, therefore, that these unusual appointments to the chairs of pathology may account for the dissatisfaction with morphological pathology rather than a deficiency in the autopsy procedure. For the above reason, it is also understandable that the prime motivating force in many of our pathology departments is research. No one denies that research should be a fundamental adjunct to the departments of pathology, but why must it interfere and often replace the teaching and training required for young pathologists? Clinical department heads, by contrast, seem to be capable of maintaining the proper equilibrium between research and the essential training of men in their particular clinical fields. Pathologists do utilize postmortem material for research, as well as for statistical purposes and reporting of rare types of specimens. They are also well aware of the many limitations in applying and interpreting pseudophysiological studies on tissues after death.

We pathologists are not without blame for permitting this deplorable situation to arise in our profession. It is my opinion that the American College of Pathologists has been somewhat lax in not forming closer ties with our schools and serving in an advisory capacity for appointments to the chairs of pathology as well as in the teaching of pathology. The unfortunate allocation of surgical pathology, obstetric and gynecologic pathology, and neuropathology to the clinical divisions that has been occurring especially in our eastern universities tends to reflect the indifference of the heads of pathology in recognizing and maintaining high standards in their departments. Undoubtedly, one of the reasons for the shortage of men going into pathology as a specialty is the poor impression they receive as medical students when the professor of pathology is too busy with research or administrative work to teach. Our standards of pathology must never be lowered, because pathology is a specialty of the practice of medicine, as well as a fundamental basic science in the study of medicine.

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To the Editor:—I read with great interest the guest editorial "Potential Values of the Autopsy Today," as published in the March 31 issue of THE JOURNAL, and was very much disturbed by its tenor. Dr. Starr maintains that the decline of interest in the autopsy, which he has experienced in his own institution, seems "typical of what is taking place throughout the United States." I for one have not noticed this decline, and from my contacts with my colleagues in pathology as well as with many clinical conferees I have the impression that there still is a wholesome respect for the value of the autopsy for the advancement of medicine. It has not "become harder and harder for me to find young men interested in performing the routine autopsies." During the 28 years while I was in charge of the department of pathology at the Mount Sinai Hospital in New York City I trained at least 200 young physicians who spent one year in pathological anatomy in preparation for a clinical career in medicine or surgery, and the number of annual applicants has not decreased since the end of the war, although the two years of service in the armed forces have prolonged the period before establishment in practice. Since my own experiences differ from the basic observations of Dr. Starr, I cannot agree with a generalization of his assertions and suggestions. But beyond that I do not share Dr. Starr's evaluation of what he calls "the great pathological school." Were the members of this school really "content with the description of what they saw," and "was experiment alien to almost all of them?" Does this statement apply to Virchow, who in the introduction to his classic experimental article on "the obliteration of the pulmonary artery and its consequences" wrote "it would be unfortunate if Anatomical investigation would be limited to the dead material, the observation of final states . . . if its entire result would be description and classification of certain natural historic objects. The experiment is always the sure control for the pathologic anatomic conclusion." And does Rokitansky deserve the characterization that experiment was alien to him, he who was responsible for creation of chairs of experimental pathology in all the medical schools of the Austro-Hungarian monarchy? And is Ludwig Aschoff, certainly a member of the great pathological school, included in the assessment? Aschoff, whose own experimental investigations, and those of his school, have thrown light upon so many problems of human pathology. But Aschoff was aware that observational and experimental pathology are inseparable and expressed this credo in the first of his *Vorlesungen ueber Pathologie:* "He who as a Pathologic Anatomist neglects the Autopsy and puts his faith in experimental Pathology has built on sand," and "He who abandons the autopsy leaves the foundation upon which true Pathologic Anatomy has been built." Has this pathological era actually "drawn to an end?" Dr. Starr is "not aware of any research coming from studies being made at routine autopsies at present." May I remind him of the discovery of a hitherto unknown malady, fibrocystic disease of the pancreas, based primarily upon the investigations of routine autopsies by Dorothy Andersen in 1938; of the intriguing syndrome of metastasizing carcinoid and right ventricular endocardial fibrosis; and of the increasing significance of exact autopsy studies for the explanation of perinatal deaths? Must I point out that the results of experimental investigations of the pathogenesis of rheumatic fever must still be checked with exact comparative studies of the human rheumatic heart and that the source for such research must be found in the accumulated "mass of material?" Can it not be expected that autopsy tissues investigated with the ever-improving methods of modern histochemistry and eventually with the electron microscope will disclose information of strategic value? I can understand that release from autopsy responsibilities will add time for experiments, but I believe that my colleagues in pathology, who are supposed to be leaving the sinking ship of autopsy pathology, still feel quite confident on deck and will prefer to divide the available time.

Finally, Dr. Starr complains about the antiquated autopsy technique and has suggestions for improvement. No experienced pathological anatomist feels himself bound to slavishly following the traditional technique, and Virchow himself in his book on *Sektions Technik* advocated appropriate variations if the anatomic lesions can be better revealed. The recommendation of restricting the aim of the autopsy to "securing information of immediate utility to the clinicians in charge of the case" would, in my opinion, be a decided step backward, because unexpected anatomic findings are not uncommon even today in the era of exhaustive clinical and laboratory investigation of the patient. The suggestion of turning the performance of the autopsy over to the physicians and surgeons personally interested in the case is so impracticable that I prefer not to discuss it in detail. But I regard this suggestion as an insult to the professional dignity of the pathological anatomist. Raised in the tradition of the Vienna School, I have always cherished the cooperation of pathological anatomy with clinical medicine and surgery. I have tried to understand the problems of my colleagues and have considered the autopsy as a part of the clinical examination to which the pathological anatomist must contribute his share. And so, I know, have felt all my colleagues in this important discipline of medicine. For many years have we utilized, within the legal limitations, the pathological material for special investigations, suggested by our functionally minded clinical advisers. We have perfused hearts and other organs with radiopaque substances, we have inflated lungs in order to obtain appropriate x-ray pictures for comparison with the state during life, we have measured the perfusion time of atrophic kidneys and livers, we have willingly given opportunity for every procedure that could throw light upon clinical problems. I sincerely believe that the autopsy pathologist is conscious of his obligations and willing to do everything to improve upon his service to medicine according to the motto: *Hic locus est ubi mors gaudet succurrere vitae.*

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To the Editor:—It is unfortunate that there was published in THE JOURNAL of March 31, page 1144, the guest editorial entitled "Potential Values of the Autopsy Today." I use the term "unfortunate" because I am convinced that the autopsy serves as useful a purpose today as it ever did and indeed hold strongly to the opinion that it contributes to the advancement of medicine in significant degree. It is also "unfortunate" in that it appeared at about the same time as an excellent article in a widely circulated lay magazine in strong support of the autopsy. The tenor of this editorial is such that the hasty reader might readily misunderstand the attitude of the author and therefore might well be indisposed to request or urge the performance of an autopsy.

There are a few special items that deserve comment. The regulations in Austria were promulgated by the Empress Maria Theresa rather than an unnamed emperor. There was no decree that everyone dying in the General Hospital in Vienna would be the subject of an autopsy. Objections on the part of custodians of the body prevail. The present professor of pathology spends a considerable time in persuasion of those who object. I doubt that the clinicopathological conference is the last word in undergraduate teaching. A distinction should be made between an exercise of value to medical students and one of value to graduate physicians. Certainly the conference can serve both purposes, but its major impact is on the graduate physician.

There is an element of truth in saying that the experienced pathologist has a certain skepticism as to the many features of therapeutics. With the advent of modern agents such as the antibiotics, the antimicrobials, and drugs with special therapeutic action, this attitude, insofar as it ever existed, has changed materially. While the pathologist is often thought of as devoting himself entirely to morphological disorders, there can be no doubt that he is familiar with and sympathetic to the study of emotional disturbances and functional diseases. Nevertheless, when he performs an autopsy on a patient given a diagnosis of psychoneurosis who really dies with a brain tumor he naturally emphasizes the importance of precise diagnosis. That there is an increased reliance on experiment as a means of acquiring medical knowledge is unquestioned. However, experiment is a means rather than an end. It is a tool to explain processes of disease and of therapeutics. In the school from which the editorial stemmed, a professor of pathology, Simon Flexner, was distinguished as an experimental worker. At the same time, however, he performed autopsies with the most meticulous care. I am sure that in his mind there was no conflict between study of morphology and the study of function. Indeed, the two complement each other.

I take strong exception to the statement that the keenness, audacity, and mental caliber of the personnel performing autopsies today have declined greatly from the levels of the previous generation. In a large experience in such matters I would maintain that the contrary is the case. I have seen young men develop skill in the performance of the autopsy, knowledge as to the conditions observed, and the greatest interest in comparing what has been observed clinically, what the patient has lived with, and what has led to his death. To say that the routine of autopsies has not advanced since the days of Virchow and Rokitansky is not true. Even if it were, the recorded observations of these great pathologists are monumental. Similar comment should be made of the records of Osler in the Philadelphia General Hospital, made while he was a member of the faculty of the University of Pennsylvania.

To suggest that an autopsy should be simplified so that it yields information of immediate utility to the clinician in charge of the case ignores the value of the complete postmortem examination. In the interpretation of the observations, a knowledge of the details of morbid anatomy is not an end in itself but a medium for the correct interpretation of disease processes. The experienced pathologist realizes that he must have many microscopic sections if his interpretations are to be thorough.

Undoubtedly, opportunities may be seized at the time of the autopsy to study certain functional disturbances, particularly if they are dynamic. There are, however, some practical aspects to be considered in this connection. The dignity of the individual demands that the body and all its parts be handled with respect and care. Its most useful purpose is served by skillful performance of an autopsy. It is the duty of the pathologist to see that the body is repaired completely and that it is turned over to the undertaker promptly and in excellent condition.

Many pathologists whom I have consulted since the appearance of this editorial concur in the opinion that the matter of autopsies should be approached on a positive basis rather than on what appears to be a somewhat iconoclastic attitude. The future of medicine is bound in with that of pathology, and it behooves all concerned to forward the training of pathologists. The autopsy is one of the most important aspects of this training. The senior pathologist should use it for training of both assistants and students.

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To the Editor:—In a sense, as Dr. Starr's guest editorial in THE JOURNAL, March 31, stated, the method of performing the autopsy has not changed since Virchow. Neither has the method of studying a patient. But just as the latter has become fortified by a wide variety of new accessory methods, so all the new aids are available to the pathologist, if he is interested in pathology and will use them. Postmortem radiological studies, determination of physical constants, photographic methods, perfusions and injections, and above all histochemical methods are available and are used; I have myself used every one of these and others. Especially noteworthy is the field of histochemistry, which has blossomed wonderfully in the last years and will probably bloom forth remarkably in the next few. What is electron microscopy but morphology? I venture timidly to suggest that it would be to everyone's advantage if more electron microscopes would be made available to pathologists instead of to the Johnny-come-latelys to morphology who now get them. There can be little doubt that the potential value of the autopsy

today is as great as ever. One has only to watch the few remaining master pathologists to see this. Are there many contributions from clinical chemistry or physiology that are of more importance than Klemperer's formulation of the concept of collagen diseases? In my own small (and not very modest) way, I have had the satisfaction of hearing it said: "I never knew pathology could be like that." Nevertheless, Dr. Starr's description of pathology as it is today is for the most part true. If it is true and if it need not be true, something is wrong and that something needs correction.

The main thing that is wrong with pathology is that pathologists no longer teach it. Let us be blunt but honest. Money goes for "research"—not for teaching, not for routine pathology or even for vivid pathology. The professor of pathology is likely to be chosen because he has done or is interested in "research." Often he is disdainful of the old anatomic methods; not infrequently he knows little or nothing about them. Today he is likely to be so young that he has not yet performed the 100 autopsies Dr. Starr was required to do as an internist; and, since he has no use for the method, it will take him a long time as a professor before he reaches the 100. Dr. Starr has probably given an exact description of his professor of pathology and of many others. They no longer want to be responsible for routine autopsies because they do not see anything in them. But that does not mean a pathologist would not see a good deal. Imagine what would happen to surgery if the only people available for surgical chairs were those who did not see much in surgical therapy.

There is nothing wrong with animal experimentation; it has been and will continue to be useful. But it is not pathology, and its exponents are not pathologists. The view medical students get of pathology is a distorted one. They no longer gather around the autopsy table, because they have been taught that it no longer is very essential. They avoid training in pathology because they have been told the "new" experimental methods are more important. Then they become professors of pathology—and the circle is complete. The remedy is to turn pathology in the medical schools back to pathologists. Let departments of experimental medicine be created for those who prefer to study medicine in lower animals. But not until a whole generation of students has again come in contact with vital pathological anatomy can we expect to see this still important discipline take its place once more in the forefront of medical advance.

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To the Editor:—Dr. Isaac Starr's guest editorial, "Potential Values of the Autopsy Today" (*J. A. M. A.* **160:**1144 [March 31] 1956), brings up certain problems that merit further consideration. According to Dr. Starr, autopsies are done badly at his hospital and the caliber of personnel doing them has declined greatly. He presents no evidence that this has occurred elsewhere. On the contrary, I believe that the performance of excellent routine autopsies is almost universal. Dr. Starr states "the morgue is swamped with routine material." He goes on to attribute this partly to the increase in autopsies and partly to shortages of prosectors. To quote from his editorial, "the professor of pathology . . . became interested in experimenting. Soon the behavior of neoplasms in experimental animals began to absorb his attention, and his interest in the autopsies waned steadily. As time passed it became harder and harder for him to find young men interested in performing routine autopsies. . . . What wonder that the new professor of pathology in my school, an expert experimenter, has washed his hands of the whole business and has declined to be responsible for the routine autopsy service any longer."

Perhaps this is the crux of the matter. When the professor of pathology becomes in fact the professor of experimental oncology, he no longer attracts budding pathologists to his department. Very logically he attracts aspiring experimental oncologists to whom human autopsies and their clinical correlations offer no interest. Therefore, a shortage of house staff in pathology ensues. One could predict that, if the professor of surgery lost his interest in operations and "washed his hands" of them, he would soon lose his interns. Would he then demand that operations be speeded up, delegated to general practitioners, or inadequately recorded so that he might carry on his experiments? Yet these are approximately Dr. Starr's solutions to the analogous problem in pathology. I do not believe that he has adduced any real argument that the autopsy as a technique is useless or outmoded or requires change. What he has done is to point out that, in a department not interested in the autopsy as part of clinical medical practice, good autopsy surgeons and good autopsies soon disappear. Finally, to advance my own beliefs very briefly, I feel that the autopsy is an enormously useful weapon for educating physicians and raising standards of medical care. As such it needs no apologies for its forms or techniques. Use of the dissected body for additional experimentation is indeed meritorious but is not a substitute for standard techniques.

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To the Editor:—I was rather startled to read the obituary of the field of pathology by Dr. Starr in The Journal, March 31. Being a member of the allegedly vanishing species, up to the moment of reading of my demise, it had not occurred to me that I was dead. As a pathologist, reared in the morphological school, may I claim that the autopsy room is not the morgue but the center and inspiration of constantly expanding research activities. The modern morphologist infuses functionalism into the wonderful morphological base of the past. The autopsy room is the source of his problems in histochemistry, physiological pathology, and correlative medicine. I am amazed that any pathologist or teacher of pathology would want to separate himself from the source of his material and problems. The field of morphological pathology is far from being dead; it is being reborn in a greatly expanding form and requires the greatest acumen, ability, and training on the part of the young pathologist. We younger morphologists can only regret that we lack the knowledge of the autopsy held by our predecessors.

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EFFECTS OF RAUWOLFIA SERPENTINA

To the Editor:—We would like to draw attention to a discrepancy in the lead summary of our article, "Central Nervous System and Cardiovascular Effects of Rauwolfia Serpentina," that appeared in the Feb. 25, 1956, issue of The Journal, page 622. This summary was not prepared by us, nor did we have the opportunity to review it prior to publication. The major point in question is the statement in the summary that "in 15 patients with angina pectoris the alseroxylon seemed to be no more effective than the placebo preparation." Our findings, as presented in the text of the article, were quite to the contrary. In the second paragraph on page 626 we stated that "12 of the 15 subjects had improved with therapy." Table 2 on the same page illustrates in more detail the therapeutic responses of these 15 subjects. Furthermore, in the addendum on page 628, we pointed out that two of the three subjects who had not shown an early response to treatment had since distinctly improved and, as our concluding statement, we emphasized that "all but one of these 15 subjects appeared to benefit from alseroxylon therapy." We believe it is important to correct the erroneous impression left by the lead summary of this article.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

A Comparative Study of the Treatment of Essential Hypertension: The Effect of Rauwolfia and a Rauwolfia Compound (Rauwolfia, Mannitol Hexanitrate, and Rutin). S. Stonehill. A. M. A. Arch. Int. Med. **97:**189-193 (Feb.) 1956 [Chicago].

This study is concerned with the hypotensive effect of the powdered whole root from Rauwolfia micrantha alone and when combined with rutin and mannitol hexanitrate (Maxitate). Seventeen patients with moderate to severe hypertension were observed for one year. Three types of tablets of identical appearance were used. One type, labeled 7-71, contained 30 mg. of Rauwolfia micrantha; the placebo was labeled 7-72; and the third tablet, labeled 7-73, contained the following: 30 mg. of Rauwolfia micrantha, 30 mg. of rutin, and 30 mg. of mannitol hexanitrate. The contents of the tablets were unknown to the investigator throughout the study. The dosage was two tablets four times daily. The first patient studied was started on 7-71, the second on 7-72, and third on 7-73, the fourth on 7-71, and so on. At the end of six months those patients receiving 7-71 were given 7-72 and those on 7-73 were given 7-71 without their being aware of the change. It was found that mannitol hexanitrate with Rauwolfia compound has a greater hypotensive effect than Rauwolfia alone. The placebo can also reduce blood pressure, but not to the extent of the specific drugs. More than two-thirds of the patients treated with Rauwolfia or mannitol hexanitrate with Rauwolfia compound had an adequate clinical response. No serious toxic effects were noted. While taking Rauwolfia the patients felt calm and free of anxiety. Many complained again of nervousness when, unknown to them, the placebo was substituted. For this reason, it is felt that Rauwolfia should not be denied those hypertensive patients who do not get an actual fall in blood pressure. Failure to secure a hypotensive effect was observed in those patients whose hypertension was severe and of long standing and who had advanced arteriosclerosis.

Infections with Antibiotic-Resistant Staphylococci: Part 1. Results of Sensitivity Tests in Staphylococci of Various Origin. W. R. O. Goslings, Tio Liong Hien and A. W. Bots. Acta med. scandinav. **152:**439-449 (No. 6) 1955 (In English) [Stockholm, Sweden].

The sensitivity of strains of Micrococcus (Staphylococcus) pyogenes var. aureus to penicillin, streptomycin, chloramphenicol, chlortetracycline (Aureomycin), and oxytetracycline (Terramycin) was tested in the clinical laboratory of the University of Leyden, Netherlands. Three groups of strains were studied. One group of strains was isolated from patients who were hospitalized between 1947 and 1949, i. e., before broad-spectrum antibiotics were used regularly at the University Hospital of Leyden; these strains had been stored in a lyophilized state. The second group of strains was isolated from patients who were hospitalized between 1952 and 1953. The third group of strains was isolated from residents in a rural district who were private patients of one of the authors. Results of the sensitivity tests showed that the rate of resistance to streptomycin of micrococci isolated from hospitalized patients increased from about 15% in the years between 1947 and 1949 to 45% between 1952 and 1953. The rate of resistance to penicillin increased from 13% to 70%. Resistance to chloramphenicol, chlortetracycline, and oxytetracycline was absent in the strains isolated from hospitalized patients between 1947 and 1949, but about 20% of the strains isolated from hospitalized patients between 1952 and 1953 were resistant to chloramphenicol and 15% to the other two antibiotics. Five of the 100 strains isolated from hospitalized patients between 1952 and 1953 were resistant to all five antibiotics. In strong contrast with the data for the hospital strains, the resistance rate for penicillin in 50 patients with micrococcic infections in the rural practice was only 4% as late as 1953. Resistance to any of the other four antibiotics was completely absent among the patients in the rural practice. The same contrast was revealed in 55 strains isolated from the blood of patients with deep-seated, severe generalized infections (sepsis or acute osteomyelitis) if they were divided into two groups according to the origin of the infection, i. e., 47 strains with a source of infection outside the hospital sphere and 8 strains with a source of infection inside the hospital sphere. Strains resistant to antibiotics other than penicillin were detected only among the hospital strains resistant to penicillin. Hospital strains sensitive to penicillin were mainly isolated within the first two weeks after hospitalization (75% in the first five days, 80% in the first two weeks); strains resistant to antibiotics were detected mainly after the second week of hospitalization (75%). The sensitive micrococci isolated within the first two weeks after hospitalization probably represent the sensitive microflora brought into the hospital from outside by the patients themselves. The fact that only a few sensitive strains were isolated after 14 days of hospitalization shows that these strains are probably not able to survive in the hospital microflora for a long time. This may be due to the fact that they are eliminated during circulation in the hospital, when passing through patients who are receiving penicillin therapy for any other disease. The higher the frequency index with which penicillin is used, the shorter the life span of the penicillin-sensitive strains will be and the more the equilibrium in the microflora will shift to the penicillin-resistant micrococci. Resistance to the other antibiotics, which is present almost exclusively in penicillin-resistant strains, may be explained by the fact that only these strains circulate long enough in the hospital to become resistant, by degrees, when passing through patients treated with these other antibiotics. The problem of antibiotic resistance in infections with micrococci in hospitalized patients is the result of the closed community formed by the micrococcic flora of the hospital under the influence of antibiotic therapy. Outside the hospital the chances that such a closed community will develop are much smaller; the frequency index of antibiotic therapy will be low in regard to the large number of healthy persons, and after discontinuation of antibiotic therapy there will be a much larger mixing of the microflora in the patients with strains from the large natural reservoir of sensitive micrococci in the world outside the hospital than in hospitalized patients.

Clinical Value of Simultaneous Determinations of Copper and Iron in Blood Serum. J. M. Palacios Mateos. Rev. clín. españ. **69:**78-82 (Oct. 31) 1955 (In Spanish) [Madrid, Spain].

Simultaneous determinations of copper and iron in the blood serum of 15 normal persons and 47 patients were made. The values of copper and iron in the blood serum of normal persons obtained by the authors were in agreement with those previously reported in the literature. The following changes were observed:

The place of publication of the periodicals appears in brackets preceding each abstract.

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In patients with epidemic hepatitis iron is greatly increased, whereas copper is normal or slightly increased. In patients with posthepatitic or Laennec's cirrhosis, copper is greatly increased, whereas iron is normal. In patients with obstructive jaundice the values of copper and of iron do not change. The results indicate the value of the changes of copper and iron in the blood serum for the differential diagnosis between epidemic hepatitis, Laennec's cirrhosis, and obstructive jaundice. The following changes were also observed: Increase of copper and normal values of iron in the blood serum of patients with hereditary atrophy of the optic nerve (Leber's optic atrophy), increase of both copper and iron in hematochromatosis, lowering of copper with normal values of iron in progressive hepatolenticular degeneration (Wilson's disease), increase of copper in infections and in nephritis, and lowering of iron with normal values of copper in patients with posthemorrhagic anemia, digestive tumors, nutritional diseases, chronic lymphocytic leukemia, and in the course of Ca-EDTA therapy of lead poisoning.

PEDIATRICS

Infantile Cortical Hyperostosis: Report of 17 Cases. G. G. Cayler and C. A. Peterson. A. M. A. J. Dis. Child. **91:**119-125 (Feb.) 1956 [Chicago].

In the past six and a half years 17 cases of infantile cortical hyperostosis were observed in 11 girls and 6 boys between the ages of 7 and 30 weeks who had been admitted to the Children's Hospital of the East Bay in Oakland, California. There was an average period of two weeks between the onset of symptoms and the establishment of the diagnosis of infantile cortical hyperostosis. Swellings about the face were the chief signs in 13 patients. Among the many initial diagnoses entertained were idiopathic parotid swelling, syphilis, undisplaced fracture, brachial plexus injury, malignant bone tumor, blocked tear duct, parotid tumor, mumps, cellulitis of the face, paralysis of the arm, and trauma. Ten patients had low-grade fever. Tender swelling was almost always observed. Warmth and redness of the skin or enlarged lymph nodes were rare. Irritability was frequent. The average white blood cell count was 23,000, with a range of 11,300 to 37,600. The average ratio of polymorphonuclear cells was 44%, with a range of 27% to 70%. The incidence of involvement of bones was as follows: mandible in 13 patients, humerus in 6, ulna in 6, clavicle in 5, ribs in 5, radius in 4, tibia in 4, femur in 3, scapula in 3, and fibula in 3. In six patients only the mandible was affected, and in two the scapula was involved as an isolated bone. Clinical swelling was always accompanied by x-ray changes. Minimal mandibular changes often were apparent only on the oblique lateral projection. Infantile cortical hyperostosis can be confused with a variety of diseases. It should be thought of as a possible diagnosis for any firm tender swelling of the face that occurs during the first six months of life. The diagnosis of infantile cortical hyperostosis is readily made by a correlation of the clinical, laboratory, and roentgen findings. The roentgen finding of subperiosteal new bone formation indicates a nonspecific change, but when it involves the mandible of a young infant it is almost always caused by infantile cortical hyperostosis. The etiology of infantile cortical hyperostosis is unknown. There is at present no established specific therapy. The course of the disease is usually benign and self-limited.

Glycogen-Storage Disease: A Study on the Effect of Sodium *l*-Thyroxine and Glucagon. N. Koulischer and D. E. Pickering. A. M. A. J. Dis. Child. **91:**103-112 (Feb.) 1956 [Chicago].

Three cases of the hepatic form of glycogen-storage disease (von Gierke's disease) are described in baby girls aged 10, 8, and 9 months, respectively, when admitted to hospital. The first two patients were sisters. Metabolic studies, including four-hour glucose and galactose tolerance tests, epinephrine tolerance tests, insulin sensitivity tests, glucagon tolerance tests, and repeated fasting blood sugar determinations, were performed before and after a six-week course of sodium *l*-thyroxine therapy. Pronounced insulin sensitivity and relative unresponsiveness to the administration of epinephrine and glucagon was observed in these patients. Analyses of fasting blood sugar specimens revealed that a large ratio of their total reducing substance was nonfermentable and also showed their tendency to hypoglycemia. The patients were placed on a high-protein, galactose-free diet to provide the maximum possible caloric intake from protein and to avoid carbohydrates that can be utilized only after conversion in the liver. Sodium *l*-thyroxine in tablets of 0.1 mg. was administered daily orally to increase phosphatase activity. The administration of this drug for six weeks was associated with a significant disappearance of the nonfermentable reducing substance in the blood, with a corresponding increase in fermentable reducing substance. Moreover, sensitivity to insulin was reduced. A one-week course of glucagon administration during sodium *l*-thyroxine therapy was followed by an exaggerated short-term response to that substance. The high-protein, galactose-free diet was found to be of value in the management of von Gierke's disease.

Constitutional Precocious Puberty in the Male: Report of Three Cases. E. C. Jungck, N. H. Brown and N. Carmona. A. M. A. J. Dis. Child. **91:**138-143 (Feb.) 1956 [Chicago].

Three cases of constitutional (familial) precocious puberty, a rare entity, are described in an 18-month-old boy and in two 4½-year-old boys. The precocious puberty was caused by a premature gonadotropic hormone stimulation, as evidenced by the normal hormonal values for the age of the patients and the enlarged mature gonads. Thus, they fall into the classification of true familial precocious puberty. The first two patients differed from those previously reported on in that, whereas the male only was affected, the genetic transfer from generation to generation was accomplished by female carriers only. In the third patient, the genetic transfer was accomplished by both males and females. In one patient, mature sperms were found in the testicular biopsy. Differentiation of true precocious puberty in the male, which is accompanied by normal or high androgen levels for that age group, must be differentiated from the incomplete or virilism type, which is accompanied by higher than normal levels of androgenic hormones. Removal of the abnormal tissue is indicated in the virilism type, whereas true precocity is characterized by normal tissue functioning prematurely, and removal of the normal tissue is not indicated.

THERAPEUTICS

A New Medical Adjunct to the Treatment of Alcoholism: The Use of Reserpine (Serpasil). R. C. Grandon, W. Heffley, T. Hensel and S. Bashore. Am. Pract. & Digest Treat. **7:**231-234 (Feb.) 1956 [Philadelphia].

Thirty-five chronic alcoholic patients were treated with reserpine (Serpasil) during acute episodes. Most of the patients were hospitalized for a few days, with the remainder being treated as outpatients. The optimum procedure is to initiate treatment with intramuscular administration of 2.5 mg. of the drug, with the patient under careful observation, and to start oral administration the same day or as soon thereafter as possible with 0.25 mg. of the drug given three to four times daily. Injections can be discontinued within two or three days in most patients, with oral maintenance adjusted at the level found best for the individual patient. The use of reserpine according to this schedule permitted good control of most patients, with the necessity for giving barbiturates, chloral hydrate, or other sedatives greatly reduced or eliminated. Psychomotor overactivity and hostility were relieved without impairment of consciousness and with decrease of vomiting, nausea, and anorexia. Normal sleep without bedtime sedation was achieved in most of the patients, and patients were more sociable and interested in their surroundings and hospital companions. Tremors were decreased except in patients with paralysis agitans, in whom tremors often increased temporarily despite good response otherwise. Tachycardia and hypertension were also relieved. Reserpine therapy

was effective in any type of alcoholism studied, including symptomatic drinking and primary or secondary addiction. It aborted delirium tremens in two patients and terminated drinking sprees that otherwise probably would have continued in several outpatients. There was lessening of the compulsion to return to drinking in some, with improved ability to drink moderately and stop in others. Side-effects, consisting of generalized skin flushing and conjunctival injection especially after parenteral administration, gastrointestinal discomfort, looseness of stools, and dizziness or lightheadedness, were not considered serious in any case. The authors were impressed with the ability of reserpine therapy to improve and simplify the management of at least the acute phases of chronic alcoholism. Even though careful observation is necessary, especially during parenteral treatment, the over-all result is one of lessened time demands on the physician and nursing staff, with much better returns for the time that is expended. This means that more patients can be treated more effectively in the long run, with shorter hospitalization.

Prantal in Long-Term Anticholinergic Therapy. J. A. Riese. Am. J. Digest. Dis. **1**:31-34 (Jan.) 1956 [New York].

Twenty-six patients with gastric or duodenal ulcer were selected for a comparative study of the effects of three of the drugs currently used in anticholinergic therapy of peptic ulcer. Twenty-one patients had duodenal ulcers and five had gastric ulcers. All 26 patients had moderate to severe pain at the start of treatment. Six vomited persistently. Initially all 26 patients were treated with propantheline bromide (Pro-Banthine). This drug completely relieved or controlled pain in 20 of the 26 patients. Later the 26 patients were treated with methscopolamine bromide (Pamine), and pain disappeared in 22 patients and was partially relieved in 2. Two patients reported aggravation of pain. The third drug used by all 26 patients in this series was diphemanil methylsulfate (Prantal). The usual dosage was one 100-mg. Prantal tablet four times daily. In patients with severe pain, a dosage of 200 mg. was used four times daily for one or two weeks, or until the severe pain was relieved. The dosage thereafter was maintained at 100 mg. four times daily until freedom from pain was achieved, usually for about two months. Prantal relieved pain completely in 22 patients, partially in 2, and aggravated ulcer pain in 2. No side-effects were reported by or elicited on questioning of 24 patients. Dryness of the mouth occurred in two patients. Prantal was slightly more effective than both propantheline bromide and methscopolamine bromide in relieving pain and could be continued at effective dosage levels for longer periods without causing severe side-effects.

PATHOLOGY

Familial Multiple Myeloma. L. A. Nadeau, S. I. Magalini and M. Stefanini. A. M. A. Arch. Path. **61**:101-105 (Feb.) 1956 [Chicago].

The authors present histories of a man and his sister, aged 67 and 66 years, respectively, in whom the diagnosis of multiple myeloma was definitely established. Analysis of the records available at the hospital indicated that the father of these two patients probably had died of multiple myeloma. Studies were made on nine "healthy" members of this family. They included physical and urine examinations, complete blood counts, determination of erythrocyte sedimentation rate, and serum electrophoretic patterns. All tests were normal in eight of the nine subjects examined. One member, a woman, aged 60, and a sibling of the two patients in whom the diagnosis of multiple myeloma had been definite, was found to have an elevated blood sedimentation rate (48 mm. in one hour, Westergren) and abnormal serum electrophoretic pattern with increase of the serum α-globulin and β-globulin fractions. The literature has stressed the occurrence of multiple myeloma in families with high incidence of other forms of malignancy. This instance is the first documented example of multiple myeloma in members of the same family.

Tuberculous Lesions Associated with Bronchial Cancers: Anatomic Study. J. Delarue and J. Paillas. Presse méd. **63**:1788-1792 (Dec. 25) 1955 (In French) [Paris, France].

Tuberculous lesions were found in 35 of 200 anatomic specimens from patients with bronchial cancer, 27 of which had been removed at operation and 8 at autopsy. Fifteen of the tuberculous lesions were located in the pulmonary parenchyma; these accounted for 7.5% of the cases of cancer. Other workers have reported the number of tuberculous lesions of the lung parenchyma in cases of bronchial cancer to be about 7%. Nineteen other lesions were found in lymph nodes and one in a bronchus. Thirteen of the parenchymal lesions were adjacent to the cancerous bronchus. Only four of them were old, healed lesions; the others were one tuberculoma, seven cavities, two caseous pneumonias, and one tuberculous bronchiectasis. From the diversity of histological forms among the carcinomas encountered, it can be concluded that the association of tuberculosis with cancer does not depend on the type of cancer. Old, healed lesions and contralateral lesions were found only with epidermoid carcinomas. It seems unlikely that the association of the two diseases is due to chance, in view of the tuberculous lesions' being so often situated in the parenchyma adjacent to the cancerous bronchi and of the frequency of evolving forms, especially with anaplastic carcinomas. The tuberculosis cannot favor the development of bronchial cancer by chronic irritation, since the lesions are found principally not in the bronchi but in the parenchyma. It seems evident that the cancer causes the appearance of the tuberculosis or at least reactivates it.

Changes in Laryngeal Epithelium: Relation to Age, Sex and Certain Other Factors. R. F. Ryan, J. R. McDonald and K. D. Devine. Proc. Staff Meet. Mayo Clin. **31**:47-52 (Jan. 25) 1956 [Rochester, Minn.].

The studies described were undertaken to determine the differences between the laryngeal epithelium of males and of females, to evaluate the effect of increasing age, and to elaborate on the effect of certain obvious traumatic factors, such as smoking, to which the larynx is frequently subjected. The larynx, distal part of the trachea, and the main-stem bronchi were saved at routine autopsy if they appeared normal on macroscopic examination at the time of removal. Particular emphasis was placed on securing specimens from subjects 40 years of age or older. The thickness of the laryngeal epithelium was determined microscopically for the false cord, the true cord, and the subglottic area of larynxes of 60 males and 29 females. In the adult, there was no correlation between advancing age and thickness of the epithelium. The epithelium of the male larynx was thicker than that of the female. Squamous metaplasia was present in the false cord of 27 of the 60 males and in six of the 29 females and in the subglottic area of seven males and one female. The incidence of squamous metaplasia was approximately the same for all age groups from 40 to 90 years. This distribution of squamous metaplasia argues against such metaplasia being a normal occurrence of increasing age, unless such irritants as smoking cause involved tissues to age more rapidly than normal.

ANESTHESIA

Physiological and Clinical Study of an Anesthetic Steroid, 21-Hydroxypregnandione Sodium Succinate. H. Laborit, P. Huguenard, C. Douzon and others. Presse méd. **63**:1725-1727 (Dec. 14) 1955 (In French) [Paris, France].

The steroid 21-hydroxypregnandione sodium succinate has an anesthetic effect, but is more useful as a potentiator (with neuroplegics, general anesthetics, or other hormones) than as a single agent. When no premedication is used, 3 or 4 gm. of the drug is necessary to induce surgical anesthesia in a human being, and then it is often too light. The main advantage of this steroid is its low toxicity. Its effect is gentle and pleasant for the patient, and reawakening is rapid. It does not depress respiration in man. It does not disturb electrolyte and water metabolism. It has little or no influence on the vegetative periphery, nor does it affect the human cardiovascular system. The cardiac rhythm is not disturbed. Arterial pressure remains the same, and there is no important effect on diuresis.

BOOK REVIEWS

The Fields of Group Psychotherapy. Edited by S. R. Slavson. Cloth. $6. Pp. 338. International Universities Press, Inc., 227 W. 13th St., New York 11, 1956.

This valuable compilation of 19 surveys describes in detail the use of group psychotherapy in the treatment of many psychiatric conditions in various settings. The book extends and brings up to date the description of the specific uses of group psychotherapy that was covered in a previous volume ("The Practice of Group Therapy," published in 1947), which was also edited by Mr. Slavson. Practically every condition and every field in which group psychotherapy has been used is covered in the present volume. The contributors, all of whom are recognized authorities in this field, bring a wealth of experience to the work. The use of group psychotherapy in mental and general hospitals, social agencies, child guidance clinics, and private practice is described. There are detailed descriptions of the treatment of many conditions with group psychotherapy. These include "psychosomatic disorders," addictions, alcoholism, stuttering, allergies, psychiatric illness of the aged, and delinquency. There are also chapters reporting the use of this technique in the treatment of mothers with disturbed children, unmarried mothers with emotional problems, and patients with sexual and marital problems. There is a section on the use of group psychotherapy in industry and in the training of psychiatric personnel including physicians. The final section discusses research in group psychotherapy.

The contributions are unusually well written and organized and cover a great deal of material in a clear and concise fashion. Each section defines the condition or the problems under consideration and summarizes the literature relating to the etiology, pathology, and the dynamic factors involved and also the principles involved in the treatment, relating this specifically to the rationale for the use of group psychotherapy. Indications and contraindications for group psychotherapy in relation to the various types of patients and conditions are covered in each section. Descriptions of group psychotherapy in the various conditions and settings are given, with illustrations. Case histories are cited to demonstrate the effectiveness or lack of effectiveness of the treatment, with a discussion of the factors involved. Of particular interest to the physician are the sections on psychosomatic disorders, addiction, alcoholism, allergies, and geriatrics. In all of these, a vast amount of material is summarized to give a clear picture of the nature and treatment of these complicated conditions. The other sections also succeed in accomplishing this. As a result, the book provides a comprehensive view of many complicated conditions and problems requiring psychiatric treatment and indicates how an understanding of their nature leads to an effective use of group psychotherapy in their treatment. Because of its scope and thoroughness, the work can be used as a source of reference. Of equal importance is the fact that the material is presented in such a manner as to be readily understood by the physician who is not specifically trained in psychiatry.

Principles of Psychoanalysis: Their Application to the Neuroses. By Herman Nunberg, M.D. Foreword by Sigmund Freud. Translated by Madlyn Kahr and Sidney Kahr, M.D. Cloth. $7.50. Pp. 382. International Universities Press, Inc., 227 W. 13th St., New York 11, 1955.

This book, initially published in German in 1932, now makes available to the English-reading student of psychoanalysis a profound and comprehensive presentation of the psychoanalytic theory of the neurotic process by one of the ablest exponents of this branch of medical science of our day. Despite some revisions and additions made by the author, the basic content of this book is essentially the same as in the earlier work, about which Freud wrote in a foreword: "Those who seek a simplification and a glossing over of the problems with which it deals will be disappointed in this book. Those, however, who prefer scientific thinking, who appreciate theoretical formulations which never abandon their ties to experience, those who can savor the rich diversity of psychic events—those persons will value and eagerly study this work." Despite the competence of the translation, this book is not easy to read. It is not an introduction to the subject of psychoanalysis for the beginner but rather an attempt to fuse and integrate various aspects of psychoanalytic theory of both comparatively early and more recent origin into a coherent whole for the reader with broad experience in the field. Unfortunately, clarity is occasionally lacking as a consequence of the author's style, which tends to be unsystematic, repetitious, and wanting in precision. On more than one occasion, in formulating a definition he uses the word to be defined; e. g., "The general basis of anxiety is therefore an excessive augmentation of a stimulus whose excitation subsides (is discharged) through the specific painful affective eruption which is called anxiety." The presentation includes several aspects of psychoanalytic theory concerning which there is not general agreement; e. g., the postulation of a death instinct. There is a tendency, furthermore, which is in the classical psychoanalytic tradition, to weight childhood sexuality in terms of the male child and to attribute the female Oedipus complex less to biological factors than its male counterpart. The basic value of the book, however, transcends these details, and Freud's estimate of the work will be reechoed today by those who value a scientific exposition of psychoanalytic theory and practice.

Advances in Virus Research. Volume III. Edited by Kenneth M. Smith and Max A. Lauffer. Cloth. $8. Pp. 338, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10, 1955.

This volume is the third in a series concerned with the recent developments in knowledge of the properties of viruses. The 10 contributors represent some of the outstanding investigators in the field of virology in the United States, England, and France. This volume should serve as a valuable reference book for all scientists interested in the field of virus research. The topics covered are comparative biochemistry and virology (Cohen); chemotherapy of viruses (Matthews and Smith); tumor viruses (Beard, Sharp, and Eckert); morphology and development of insect viruses (Smith); multiplication of plant viruses in insect vectors (Maramorsch); cross protection between strains of yellow-type viruses (Kunkel); and current status of bacterial transformations (Ephrussi-Taylor). The topics by the various authors are presented in a uniform manner throughout the volume, so that each subject has a brief outline at the beginning, with page numbers to make ready reference possible. At the conclusion of each article, there is a bibliography listing references alphabetically by authors. There is a subject index and an author index. The three volumes should be most useful.

Introduction to Hepatic Surgery. By Henry Gans, M.D. With an introduction by A. Brunschwig, M.D., Attending Surgeon to Memorial Hospital for Cancer and Allied Diseases, New York. Cloth. $12. Pp. 265, with 120 illustrations. Elsevier Publishing Company, 2330 Holcombe Blvd., Houston 25; 118 Spuistraat, Amsterdam C, Netherlands, 1955.

In this timely monograph, many misconceptions concerning the anatomy of the liver are clarified. The author is a Dutch anatomist and has documented his observations with line drawings, color plates, and cleared specimens. An excellent review of the anatomy of the liver is presented. The chapter dealing with indications for hepatic operations stimulates one to conjecture as to the future of liver surgery. The indications for such operations are outlined in detail. The care of the patient in the preoperative period is well summarized. An excellent and complete bibliography is presented. The author writes in a clear and succinct manner. This book should serve a useful purpose in the hands of those surgeons who have met failure in hepatic surgery in the past and need stimulation prior to a second attempt. It is a book that requires study, as it is not light reading in any sense.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

LEUKOCYTOSIS DURING PREGNANCY

To the Editor:—*What degree of leukocytosis is normal in pregnancy? At the fifth month would a total count of 15,000 per cubic millimeter, with 82% polymorphonuclear leukocytes, be normal? What happens to the sedimentation rate in pregnancy?* *M.D., New Hampshire.*

Answer.—A leukocyte count up to 15,000 per cubic millimeter during pregnancy is considered normal. At the fifth month of pregnancy a leukocyte count of 15,000 per cubic millimeter, with 82% polymorphonuclear leukocytes, should make one suspect some pathology, and further studies should be done. The erythrocyte sedimentation rate is increased after the 5th to the 32nd week. Then, it drops rapidly, especially during the postpartum period.

TUBE FEEDING

To the Editor:—*I would like information on tube feeding in chronic cases as regards the length of time a tube can be safely left in the stomach, whether it should be removed at regular intervals, what the best material is, and what the size of the tube should be.* *M.D., Virginia.*

Answer.—A gastric feeding tube may be used indefinitely. It need not be removed at regular intervals but should be occasionally removed and changed from one nostril to the other to prevent discomfort. Some prefer plastic tubes, others rubber. The rubber tube may cause more trouble because of crusting. The polyethylene tube is more comfortable, being collapsed when food is not being forced into the tube; however, there is more difficulty in keeping it functioning. The size of the tube varies from 8 to 16 F. With a feeding formula, it is better to use the larger tube to prevent blocking. One should be especially careful to avoid esophagitis in patients with peptic ulcer or in those who have been operated on for ulcer. Patients with poliomyelitis should also receive some gastric antacid while having tube feeding, since gastric or esophageal ulcerations are likely to occur.

CATARACT

To the Editor:—*A man, aged 54, has an incomplete cataract in his right eye, poor vision, slight cloudiness in his left eye, and vision from 20/40 to 20/30. Despite wearing glasses he is unable to drive or do close work. While he is driving, objects appear to suddenly loom in front of him. By the daily use of mydriatics, he has been able to improve his vision, so that he is able to drive and do regular desk work. Is it safe to continue the use of a mydriatic daily or as often as is needed until such time as surgery may be necessary? If so, what is the safest mydriatic?* *M.D., New York.*

Answer.—Many individuals with cataracts that involve the visual axis find much better visual definition when the pupils are dilated. Because of the deleterious effects of mydriasis in glaucoma and the frequency with which glaucoma and cataract are associated, many ophthalmologists feel that this method of treatment is reckless. However, in an occasional patient who secures definite visual improvement, the pupil may be dilated, provided glaucoma is definitely excluded by tonometry and the progression of the cataract is carefully and frequently followed. The best mydriatic to use is probably a combination of 2% homatropine hydrobromide and phenylephrine hydrochloride (Neo-Synephrine) instilled in each eye as frequently as necessary.

COMMON BALDNESS

To the Editor:—*A 36-year-old athlete has had rapid loss of hair in the past two years to the point of baldness and a simultaneous process of graying almost to the point of whiteness. His family history is negative for baldness. He has been healthy except for a sudden recurrence of a rather quietly smoldering chronic otitis media with mastoiditis, which was interrupted by an uneventful and successful mastoidectomy. Can anything be done for this man?* *M.D., Ohio.*

Answer.—Medicine has nothing to offer in a case such as this. Though hereditary hormonal factors are thought to play a role, the precise cause of common baldness is still obscure. Only hair dyes can change the color of hair, and they may be used provided the patient tolerates them. Sensible persons do not think the results warrant the effort. Corticosteroids have been used experimentally for alopecia areata only, and, in some cases, the results were gratifying as long as they were used; however, they are not recommended for routine therapy. Steroids are not to be used for ordinary baldness.

MARRIAGE OF SECOND COUSINS

To the Editor:—*A healthy female, aged 18 years, wishes to marry her 21-year-old second cousin who is in excellent health. His paternal grandfather and her father were brothers. What can they expect as regards their offspring?*

William R. Galeota, M.D., Kerhonkson, N. Y.

Answer.—If the ancestry on both sides for three generations is sound physically, intellectually, and emotionally, there is no biological objection to the marriage of these second cousins—they are incurring practically no more danger than they would if they were unrelated.

FUNGUS INFECTION OF EYE

To the Editor:—*A patient has Microsporum canis infection of the right eye of about five months' duration. Are there any drugs that will clear up a fungus infection of the eye?*

G. P. Cassidy, M.D., Waukegan, Ill.

Answer.—Microsporum infection of the eye is relatively uncommon. From the question it is not made clear whether this infection is cutaneous or conjunctival. In view of the rarity of a pure conjunctival infection, one would assume it to be cutaneous. If such is the case, the daily application of a fungicidal ointment to the involved areas of skin should clear up the condition in three to four weeks. A preparation containing 3% sulfur in cold cream is adequate. If the brow area is involved, epilation of infected hairs may be done, although this is probably not necessary. Conjunctival infection, exclusive of cutaneous involvement, is very rare. Patients reported on have responded well to treatment with zinc sulfate.

PELLEGRINI-STIEDA DISEASE

To the Editor:—*I am sure that you will want to correct a statement that appeared in the Queries and Minor Notes section of* The Journal, *Feb. 25, 1956, page 727, on Pellegrini-Stieda disease. The answer states that this disease is a condition of the upper portion of the lateral ligament of the knee. The characteristic calcification of this condition occurs at the femoral attachment of the medial collateral ligament.*

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.